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VOLUME 217 JULY 15, 1937 NUMBER 3

CLINICAL ASPECTS OF PRIMARY CARCINOMA OF THE GALL BLADDER

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BOSTON

PRIMARY carcinoma of the gall bladder is a more frequent disease than is generally realized. Although an extensive literature pertaining to it has accumulated, the discussions are largely from the pathological and surgical points of view. It is therefore considered advisable to present an analysis of the clinical data in a group of 48 consecutive cases of primary carcinoma of the gall bladder collected from the records of the Boston City Hospital. That this disease is only rarely recognized clinically is shown by the fact that, in these 48 cases, a correct diagnosis was made in only 2. During the same period this diagnosis was made clinically eight times. In 4 cases the diagnosis was shown to be incorrect by either operation or autopsy, and in the remaining 2 cases the diagnosis was not confirmed. Each of the 48 cases was verified by operation, autopsy or both. In 31 instances the diagnosis was made at autopsy and in 17 at operation. A biopsy examination confirmed the surgical diagnosis in 11 cases. In 6 cases an exploratory operation only was performed.

INCIDENCE

The exact incidence of primary carcinoma of the gall bladder is hard to determine. Statistical data are available, but they have been collected from various points of view. Shelley and Ross[1] give it fifth place in frequency of incidence of cancer among the organs concerned with digestion, while Boyce and McFetridge[2] give it sixth place. According to Kaufmann[3] it constitutes 5 per cent of all cancers examined after death, and according to Graham[4] 8 to 10 per cent of all carcinomas in women. On the other hand, Boyce and McFetridge[2] found it in only 0.33 per cent of all autopsies and von Berencsy and von Wolff[5] in approximately 0.85 per cent. In our own series of 11,400 consecutive autopsies it was encountered 31 times, an incidence of 0.27 per cent. The incidence of primary carcinoma of the gall bladder in cases operated upon for gall bladder disease is given by MacCarty[6] as less than 0.5 per cent, by Judd and Gray[7] as approximately 1 per cent, by Boyce and McFetridge[2] as 1.12 per cent, by Erdmann[8] as 1.14 per cent, by Deaver[9] as 1.6 per cent and by Smithies[10] as 2.3 per cent. But the incidence of carcinoma in gallstone disease is given by Heller[11] as 3.34 per cent, by Gessner[12] as 4.0 per cent, by Lentze[13] as 4.3 per cent, by Graham[4] as 4 to 5 per cent, by Moynihan[14] as 5 per cent and by Riedel[15] as 7 to 8 per cent. One may therefore say that the incidence of primary carcinoma of the gall bladder in cases operated upon for cholecystitis is approximately 1 per cent, and in cases of gallstones between 4 and 5 per cent.

SEX AND AGE

All observers, with the exception of Smithies,[10] agree that primary carcinoma of the gall bladder is commoner in females than in males. In Smithies's series there were 16 males and 7 females. Ewing[16] estimates that it is from four to five times as frequent in females as in males, while Kaufmann,[3] Harley,[17] Kraus[18] and Colwell[19] believe it to be twice as frequent. Judd and Baumgartner[20] found it three times as common in females as in males. In this series there were 28 females and 20 males.

TABLE 1. *Age and Sex Distribution of Primary Carcinoma of the Gall Bladder.*

Age	Male	Female	Total
Below 40	1	1	2
40-49	7	3	10
50-59	4	9	13
60-69	5	8	13
70 and above	3	7	10
Total	20	28	48
Average Age	56.6 yr.	56.3 yr.	

Like carcinoma in any other organ, primary carcinoma of the gall bladder occurs more frequently after the age of 40. The youngest authentic case on record was in a man 22 years old. In the pres-

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ent series, the ages ranged from 26 to 84 and are shown in Table 1. The average age of the 20 male patients was 56.6 years, of the 28 females 56.3 years. If one divides the cases into those with and without stones the difference in the ages of the two groups is rather striking. Table 2

TABLE 2. *Age and Sex of Patients with Primary Carcinoma of the Gall Bladder, with and without Gallstones.*

	Stones Present		Stones Absent	
	Males	Females	Males	Females
	59	67	69	61
	48	50	47	44
	63	68	49	57
	55	66	50	47
	82	73	45	26
		60	62	45
		64	41	54
		68	53	50
		73	71	79
		59	62	72
		57	28	58
		72	42	82
		54	84	56
		72	64	
		60	43	
Total Cases	5	15	15	13
Average Age	61	66	54	55

shows these differences. No explanation is offered as to the interesting difference in the average ages of these two groups.

PATHOLOGY

It is not the purpose of this paper to dwell on the pathological aspects of carcinoma in general or of carcinoma of the gall bladder in particular. Suffice it to state that there are four distinct types of primary carcinoma of the gall bladder—papillary, scirrhous, gelatinous and squamous. Grossly, the scirrhous type is likely to produce a small, contracted gall bladder, while all the other types produce an enlarged one.

The spread of the carcinoma may be by direct extension or by metastasis. Invasion of the liver occurs early, and in later stages may be very extensive. In our group the liver showed evidences of carcinomatous invasion in 43 cases. Metastasis to the regional glands both within and behind the peritoneum is very common. This occurred in 23 cases in this series. Involvement of the extrahepatic ducts by direct extension or compression of the ducts by enlarged metastatic glands is the most frequent cause of jaundice in these cases. In 1 case, however, an incidental occlusion of the common duct by a stone caused an obstructive jaundice. The duodenum, the hepatic flexure, the transverse colon and rarely the stomach may be invaded and partially obstructed; 5 such cases were observed in this series. The portal vein may be compressed by the enlarged regional nodes, thus leading to ascites. This was noted five times. In 5 cases in this series the peritoneum was studded with metastatic carcinoma. Distal metastases have been reported: invasion of the lungs, pleurae, breasts, spine, ilium, jejunum, pelvic organs and so on. In 1 of our cases the right adrenal was destroyed by metastasis.

CLINICAL OBSERVATIONS

In the early stage of carcinoma of the gall bladder, when the changes are microscopic, there are no characteristic symptoms or signs, and the symptoms of an accompanying cholecystitis or cholelithiasis may dominate. In this series 28 patients (16 males and 12 females) had no symptoms or signs of a preceding involvement of the biliary tract, although stones were found in 7 of the males and 4 of the females. Nine patients (1 male and 8 females) gave symptoms of repeated gallstone colic, in some cases for 5 years and more. Eleven patients (3 males and 8 females) gave long histories suggestive of chronic cholecystitis. In 5 cases of this group stones were found.

With the increasing size of the tumor, symptoms and signs develop. Pain was the most frequent chief complaint. The presenting sign was jaundice in 30 cases, or approximately 60 per cent, and a palpable mass in 25 cases, or 50 per cent. Not infrequently the first symptom was that caused by a metastasis. In 2 of our cases the presenting symptoms were those of transverse colon obstruction, and in 1 case, of duodenal obstruction. In the literature there are cases reported in which the first sign was a metastatic tumor in the breast, the spine or elsewhere.

Epigastric distress, fullness, belching, constipation, diarrhea and vomiting were frequent complaints of the patients with carcinoma of the gall bladder. These symptoms, however, are not characteristic. Loss of weight was invariably present and ranged from 5 to 50 pounds. Cachexia was usually absent. The blood picture showed only a moderate secondary anemia, even in the far advanced cases. Ascites occurred in 5 cases. Fever was absent except when infection such as empyema of the gall bladder accompanied the lesion. This occurred in 2 cases.

The jaundice was almost always of the obstructive type. The icteric index ranged from 50 to above 100; the van den Bergh reaction in those cases in which it was done was direct and markedly elevated. Of the 30 cases that had jaundice, 14 had careful stool studies. Of these, 12 showed persistent absence of bile in the stools, while in 2 cases bile was noted at some time.

A palpable mass in the region of the gall bladder was observed 25 times. This mass varied in size from that of a tennis-ball to that of a grapefruit or even larger. It was usually irregular, at times pear-shaped, nodular and hard. It was not tender unless there was also present a secondary empyema of the gall bladder or an invasion by carcinomatous tissue of the adjacent peritoneum. The mass was not movable. It was usually separated from the edge of the liver by a palpable groove. The liver was frequently enlarged, hard and irregular.

Pain was present in 28 cases. It varied from severe colic resembling that of gallstone attacks to a mild but persistent pain in the right upper quadrant and epigastrium. The radiation of the pain was similar to that in gall bladder disease but in some cases the pain radiated to the left upper quadrant or lower abdomen. In most cases where colic occurred stones were found, but stones were present in the absence of colic.

Vomiting was not an important symptom, although it occurred occasionally in 26 out of the 48 cases. A gross hematemesis was observed in 1 case. In this case the autopsy revealed considerable metastatic involvement of the liver but no cancerous or ulcerous lesions within the upper digestive tract. In cases where the duodenum was invaded by the carcinoma, vomiting became an important symptom on account of the partial obstruction of the duodenum.

The bowels were usually constipated; rarely there was a diarrhea. In the presence of jaundice, clay-colored stools were the rule. In 2 cases there was a history of tarry stools. Occult blood was found in the stools of 4 cases. When the colon was obstructed by direct invasion with carcinomatous new growth, alternating diarrhea and constipation or pronounced obstipation occurred.

Loss of weight was present in every case, and in some of the advanced cases it was very marked; the average loss was 15 to 20 pounds. Severe anemia was an unusual symptom; the average red blood cell count was about 4,000,000 and the hemoglobin 65 to 70 per cent. The white blood cell count ranged between 6,000 and 10,000, and was higher only in cases where there was a secondary empyema or cholangitis.

In 1 case perforation into the hepatic flexure occurred. In 5 cases the finding of the carcinoma of the gall bladder was accidental. Four of these patients died of intercurrent disease without any signs or symptoms of gall bladder disease, the carcinoma having been found at autopsy. These 4 patients were: a female, aged 73, who died of lobar pneumonia and showed a carcinoma of the gall bladder with stones; a male, aged 48, who died of Vincent's angina and showed at autopsy the same findings; a male, aged 28, who died of pulmonary tuberculosis and showed a primary carcinoma of the gall bladder without stones; and a male, aged 42, who died of cirrhosis of the liver and showed carcinoma with no stones. The fifth patient, a female aged 26, was operated upon for acute appendicitis, and a contracted, hard gall bladder was found at operation. Suspecting a chronic cholecystitis, the surgeon removed the gall bladder, which showed on histologic examination a definite adenocarcinoma without stones.

Since carcinoma of the gall bladder is accompanied by chronic cholecystitis with the loss of concentration power of the mucous membrane, the Graham test was positive whether jaundice was present or not. Plain scout plates showed at times what was interpreted as a large gall bladder or a tumor in the region of the gall bladder, but in only 2 cases was the diagnosis of cancer suggested by the roentgenologist. Stones, when present, were demonstrated roentgenologically in 40 per cent of the cases. Other laboratory tests furnished little information. Unfortunately, none of our cases had had a diagnostic transduodenal bile drainage.

DISCUSSION

Primary carcinoma of the gall bladder is generally assumed to be a classical example of chronic irritation terminating in a cancerous degeneration. Most authors assume that gallstones predispose to cancer of the gall bladder, pointing to the frequency of its coincidence. In Judd and Gray's series, 64.6 per cent of all the patients with primary carcinoma had stones. Other statistical data on the incidence of stones in primary carcinoma of the gall bladder give even higher figures, ranging from 69 per cent (Musser[21]) to 100 per cent (Janowski[22]). On the basis of these and similar observations, Moynihan,[14] Graham,[4] Finsterer[23] and others advise removal of gall bladders containing stones in order to prevent carcinomatous degeneration.

Aschoff and Bacmeister[24] and others, however, believe that gallstones form in a carcinomatous gall bladder. Smithies,[10] Lepehne[25] and others feel that the interrelation of stones and primary carcinoma is as yet unproved. Illingworth[26] brings up the question of chronic cholecystitis being a predisposing factor in the cancerous degeneration of the gall bladder. Although this series is small, and therefore conclusions can be drawn only with considerable reservation, the evidence points against an etiologic relation between carcinoma of the gall bladder and gallstones. To recapitulate the evidence, attention should be called, first, to the lower average age of the cases without stones as compared with that of those with stones; sec-

ondly, to the sex difference—in 28 females with carcinoma of the gall bladder, 15 had stones, an incidence of 53.4 per cent, while in 20 males only 5 had stones, an incidence of 25 per cent; thirdly, in only 9 patients was there a history of previous gallstone colic, in 11 cases there was a long history of digestive disturbances suggestive of a chronic cholecystitis, while 28 gave no history of preceding gall bladder disease.

It is interesting to note that the average age of patients in whom the finding of a carcinoma of the gall bladder was entirely accidental was 45.2 years, and in this group only 2 cases showed stones. On the basis of this group, the author must agree with the opinion of Smithies and Lepehne that the interrelation between gallstones and primary carcinoma of the gall bladder is as yet unproved.

The diagnosis of carcinoma of the gall bladder may be impossible, but on the other hand it may be comparatively simple, as in cases which have a palpable, nodular, hard, immovable mass in the gall bladder region, enlargement of the liver and obstructive jaundice. In the majority of the cases the diagnosis has clinically been only suspected. Depending upon whether colic accompanies the jaundice or not, gallstone colic, common bile duct stones, carcinoma of the biliary tract, carcinoma of the head of the pancreas, and benign obstruction of the common bile duct, all must be considered in the differential diagnosis. In the cases without jaundice but with a palpable mass, carcinoma of the hepatic flexure, stomach or liver, also syphilis of the liver, must be ruled out. Finally, in the cases without jaundice and in the absence of a palpable mass, the usual diagnosis is either cholecystitis or cholelithiasis, but at times a distant metastatic lesion causing a partial obstruction of the pylorus or bowel, or invasion of the lungs or spine, predominates.

An early clinical diagnosis when neither jaundice nor a palpable tumor is present is impossible. When the diagnosis can be made with any degree of certainty, the cancer has advanced beyond the stage when surgery can do any good. Therein lies the hopelessness of the entire question of primary carcinoma of the gall bladder. Again, to remove every gall bladder containing stones in the hope of preventing carcinomatous degeneration seems unjustifiable and excessively radical surgery, especially since in 1 case of this series carcinoma of the gall bladder occurred 5 years after a cholecystostomy for gallstones without the recurrence of stones. Over 50 per cent of the cases in this series had no preceding gall bladder symptoms, and in almost 40 per cent of the cases no physician was consulted before the occurrence of the malignancy.

CONCLUSIONS

Primary carcinoma of the gall bladder is a more frequent disease than is generally recognized. The clinical diagnosis is but rarely made. When the diagnosis can be made with any degree of certainty it is usually in advanced cases beyond any surgical help. The combination of an obstructive jaundice and an irregular nodular mass in the gall bladder region is strongly suggestive of primary carcinoma. The relation of gallstones to primary carcinoma of the gall bladder is discussed, and although the possibility of an etiologic relation is admitted, it is felt that so far it has not been proved.

483 Beacon Street.

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USE OF THE GONADOTROPIC HORMONE OF PREGNANCY URINE IN THE TREATMENT OF MALE SEXUAL UNDERDEVELOPMENT

CHARLES H. LAWRENCE, M.D.,* AND ARTHUR M. HARRISON, B.A.†
BOSTON

IN the past 5 years an increasing interest has been manifested in the hormonal treatment of cryptorchidism and sexual infantilism. The present study comprises an analysis of the reported results following treatment of these conditions with the anterior pituitary-like hormone of pregnancy urine. They are further correlated with the dosage employed and the duration of treatment.

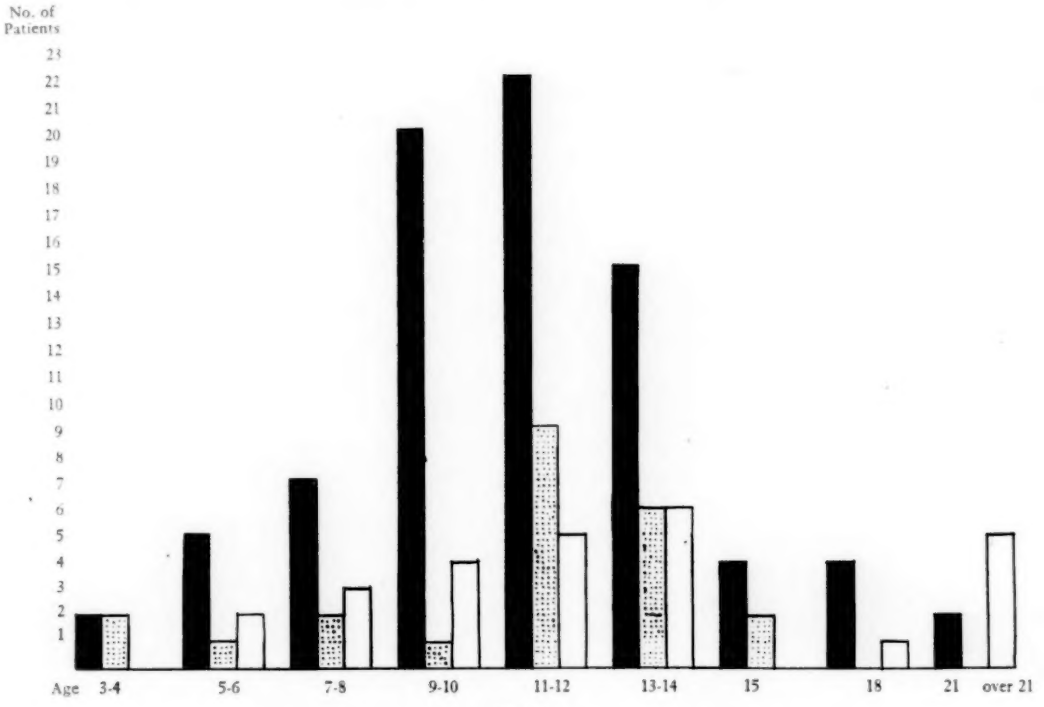

CHART 1.

The results of treatment in the entire series. The solid black columns represent patients successfully treated; the stippled columns, those in whom treatment was partially successful; the white columns, those in whom treatment was unsuccessful.

Schapiro[1] in 1930 first reported the clinical use of this hormone in sexual underdevelopment. Engle[2] clearly demonstrated the effect of gonadotropic hormones on the rat testis, and in 1932 showed that it would produce precocious descent and development of the testes of the prepubescent macacus monkey. He found further that the enlargement of the monkey testicle was due to growth of the germinal tissue and that the interstitial cell mass showed an increase in size of from four to ten fold. No acceleration of spermatogenesis was noted, however, the effect being manifested mainly by the interstitial cells of Leydig and by edema and turgescence of the scrotum and penis. These later effects were no doubt due to the increased production of testicular hormones, since they did not appear in the castrate monkey.

On the basis of Engle's findings, Goldman and Stern,[3] in 1933, announced that they had applied his methods to the treatment of 2 cases of cryptorchidism in man; and a little later Sexton[4] reported on 13 similar cases. More recently numerous other investigators have presented studies of the response of sexually underdeveloped patients to the gonadotropic hormone of human pregnancy urine.[5–17]

Only those case reports that stated the position of the testes, the status of development before and after treatment, the dosage in rat units and the duration of treatment are included in this present study. One hundred and twenty-two cases were selected from the literature as conforming to these conditions. They can be divided into three types: (1) unilateral cryptorchidism, (2) bilateral crypt-

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orchidism and (3) cases with scrotal testes which were subnormally developed. Each type, on the basis of the terminal result, may be arbitrarily subdivided into successful, partially successful and unsuccessful. The criterion for the successful group is complete descent of the testes in the cryptorchids, together with the induction of sexual development within normal limits for the age in the underdeveloped cases. The partially successful cases are those in which some response to treatment was observed, but in which complete normalization did not occur. In this group are placed cases of bilateral cryptorchidism in which descent of only one testicle occurred, and those of unilateral cryptorchidism in which a testicle not detectable before treatment entered the inguinal canal but did not descend into the scrotum. Also included are the patients with scrotal but underdeveloped testes (henceforth termed eunuchoid), in whom development did not attain normal limits. Unsuccessful cases are defined as showing a questionable response or no change.

Chart 1 indicates the age groups and response to therapy in each. It will be noted that the majority of the patients were between 9 and 14 years of age. Unilateral cryptorchidism was present in 48 per cent, bilateral in 30 per cent and a eunuchoid condition in 22 per cent.

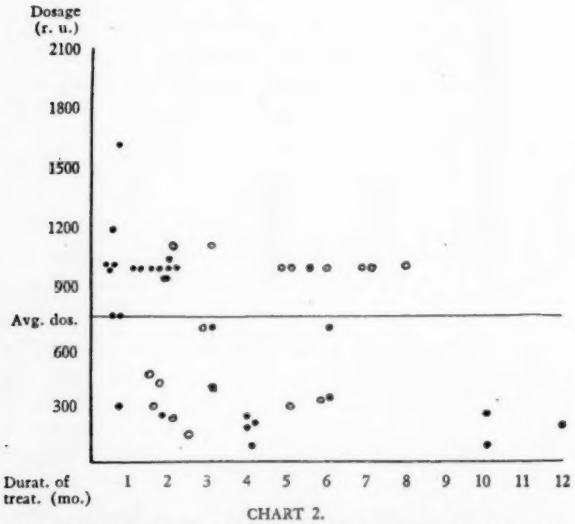

CHART 2.

Cases of unilateral cryptorchidism. The black dots represent the successfully treated patients; the circles represent failures of treatment. The cases are plotted on the basis of duration of the treatment and the dosage administered. The average dosage for the group is indicated by a horizontal black line.

An analysis of the unilateral group (Chart 2) shows 30 cases in which successful results were obtained. There were 12 partially successful and 17 unsuccessful cases. The average dosage and length of treatment in the unsuccessful slightly exceed those in the successful group, the former receiving an average dose of 740 r.u. (rat units) per week. This compares with the average weekly dose in the latter of 690 r.u. Such a finding suggests that the unit of dosage and the duration of treatment are not the only factors involved, and that the age of the patient and the presence or absence of hernias, adhesions or operative trauma may determine the results. With an increase in dosages to approximately 1,000 r.u. the proportion of successes to failures is much higher than that in cases treated with less than 400 r.u. Of the 12 partially successful cases, nearly all show evidence of definite response in the descended but little response in the undescended testicle. In regard to the duration of treatment, the response is much more rapid in the patients who receive large dosages. Over a period of the first 3 months of treatment six times as many cases responded at the higher level.

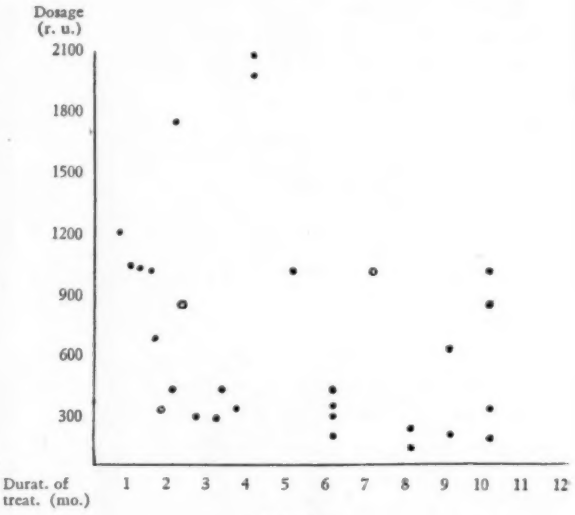

CHART 3.

Cases of bilateral cryptorchidism charted according to duration of the treatment and the dosage administered. The black dots indicate successfully treated patients; the circles, failures.

This suggests that the *intensity* of treatment rather than the total amount which the patient ultimately receives is an important controlling factor in determining the results. Five of the 17 (29 per cent) failures had been operated upon for undescended testicle, and are in the low dose level of under 400 r.u. Three cases were above the age of 21, 1 of these having been operated upon at the age of 11; the missing testicle was not found, and this patient should not be included. The high percentage of failures and of only partial successes suggests that if the retained testis does not respond to 3 months of adequate treatment there is little likelihood that it will descend without operative interference.

Study of the bilateral cryptorchid group (Chart 3) shows that 26 cases were successfully treated. Partial success was achieved in 7, and there were only 3 failures. The average dosage of 680 r.u. in the successful cases of this group is practically

the same as that employed in the successful cases of Group 1. Treatment was completed in an average of 16 weeks in the unilateral cryptorchid patients, however, as against 20 weeks in the group with bilateral cryptorchidism. In the partially successful group of 7, 4 responded with the descent of one testicle, and the 3 others showed enlargement and descent of the testes in the canal, but without complete scrotal emplacement. Of the 3 failures, one was a pituitary dwarf, aged 38, with a pluriglandular deficiency. One of the other patients received only 300 r.u. per week for 7 weeks, so that the failure may probably be charged against inadequate treatment. The reason for the failure in the third patient remains undetermined.

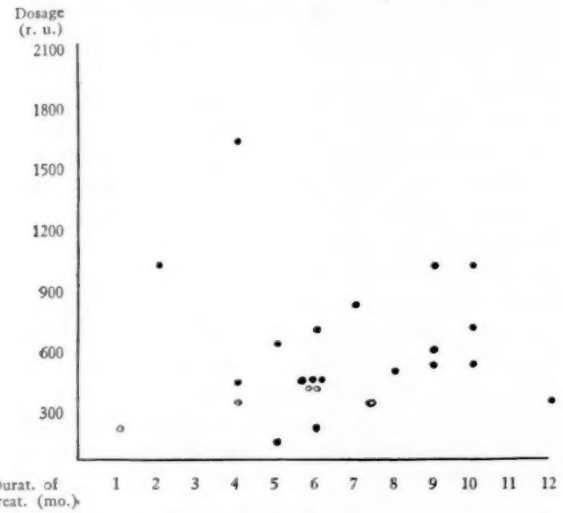

CHART 4.

Cases of eunuchoid patients charted according to the duration of treatment and the dosage administered. The black dots indicate successfully treated patients; the circles, failures.

The eunuchoid patients (Chart 4) in whom the testes are descended but subnormal are usually described by the terms, Froehlich's syndrome, adiposogenital dystrophy or simply eunuchoidism. Nineteen of these were successfully treated; 2 were classed as partially successful; and 5 were failures. The successful cases received an average weekly dose of 605 r.u. over a period of 20 weeks. In the failure group, we find a striking difference as the average dose was only 290 r.u. and the average duration of treatment 19 weeks. Insufficient treatment may, therefore, account for some of the failures. This type of underdevelopment, in all probability, represents the clearest cut picture of glandular deficiency. The majority of these patients show signs of retarded physical development in addition to sexual infantilism. This type of maldevelopment is much slower in responding to hormone therapy than simple cryptorchidism. In the cryptorchid group the desired response appears on the average within 17 weeks, whereas it required 28 weeks to bring about apparently normal sexual development in the group showing systemic evidence of pituitary hypofunction.

In the evaluation of the effects of dosage and duration of treatment it must be borne in mind that the figures represent the general trend. Individual response varies greatly since it is influenced by the age of the patient, the position of the testes when treatment is begun, the association of other symptoms of pituitary dysfunction, and the presence or absence of mechanical barriers to testicular descent.

Many of the cases considered in this study had other therapy in conjunction with the pregnancy urine extract. A large number received thyroid substance, and a lesser number the growth principle of the anterior pituitary, together with desiccated anterior pituitary substance by mouth. The effect of these adjuvants on sexual development is, however, open to question. Dorff[16] states that while thyroid substance is valuable in the correction of retardation of bony growth and of obesity, it has little effect on the development of the testicles. Likewise growth hormone produces skeletal growth but little testicular growth. This is well demonstrated by the case of Rubinstein[15] where both thyroid and growth hormone failed to produce genital development until the gonadotropic hormone was added. Lurie[18] has recently reported good results with pituitary extract by mouth. The value of such pituitary medication is a disputed point, but the balance of the evidence leans toward lack of specific activity. Certainly none of these substances have shown specific action comparable to that of the gonadotropic hormones, as reported by Engle,[2] Aberle and Jenkins[7] and many other authors.

In the evaluation of the results it must be borne in mind that spontaneous correction frequently occurs both in maldescent of the testicle and in hypoplastic development. Drake[19] examined the records of 1,641 schoolboys between the ages of 8 and 19 and found 44 nondescended testicles. Twenty-five of these descended spontaneously. Williams[20] examined 2,014 English schoolboys and found 38 with unilateral and 21 with bilateral cryptorchidism. Twenty-four of the unilateral and 14 of the bilateral undescended testes came down. Most of the spontaneous descent occurred between the ages of 11 and 16. Thus, in 102 cases of undescended testes, 61 per cent descended spontaneously. Williams concluded that treatment is not required in these cases until puberty is well advanced, and that natural descent is probable up to the age of 16.

The problem of sexual underdevelopment is, however, not simply one of testicular position. The question of normal function, both endocrine and exocrine, is far more important. It has not been proved, perhaps, that the undescended testicle in

man is always hypofunctional, but clinical experience indicates that such an association is the rule rather than the exception. Furthermore, it has never been proved that bringing about scrotal emplacement of the testicle insures its normal development. The work of Moore,[23] however, indicates that it is highly improbable that testes which are delayed in their descent for years can be as well developed functionally (or anatomically) as those which have resided in their normal site since birth. The figures of Drake[19] and Williams[20] indicate that in any individual boy with cryptorchidism, the odds are 3:2 that scrotal emplacement will be attained by the age of 16, but furnish no evidence concerning the accomplishment of functional perfection. Lawrence[21] in a recent paper has called attention to the fact that delayed adolescence, in many female patients at least, carries with it permanent failure of normal sexual development.

Confronted with an individual patient, therefore, one can hardly predict with confidence that "nature will correct the condition in time." It should be remembered also that when waiting has finally proved inefficient, the optimum time for treatment has passed. Nature probably initiates the pubertal changes between the tenth and eleventh years. At least Womack and Koch[22] were able to detect testicular hormone in boys 10 years old, and found that as early as the fourteenth year the testicular hormone excretion was "of the same order as that of normal adult males." These changes involve not only the physiologic development of the gonads, but also the changes in skeletal growth, the appearance of beard growth and the masculine voice, all of which comprise the so-called secondary sex characteristics, and are largely determined by the function of the testicle. The lack of these characteristics in an individual who has passed the normal age for their appearance imposes a severe psychologic handicap upon the patient. The hypogonadal patient usually becomes aware of his condition when the high-pitched voice, female-like wide pelvis and underdeveloped genitalia are reflected in the attitude of the normal adolescent members of his social group. He is considered "different" and not infrequently "a sissy." Lurie[25] has shown that this boy in an attempt to compensate for his deficiencies is led into a state of emotional imbalance which is associated with personality changes and behavior problems. The psychiatrist and the endocrinologist may well work hand in hand in such a maladjustment.

Crampton[24] studied 4,800 schoolboys from the point of view of physiologic age as related to the secondary sexual characteristics, and concluded that the prepubescent boy was physically and mentally inferior to the postpubescent boy of the same age. One of the most frequently noted facts in the literature is the change in the personality and attitude of the patient with cryptorchidism following satisfactory response to therapy. Thus Rubinstein[15] mentions one individual where the I.Q. was raised from 81 to 98 following treatment. When these facts are viewed from the standpoint of enabling the sexually underdeveloped boy to reach maturity physically and mentally well-proportioned, we cannot agree with Williams[20] that treatment should be withheld until the age of 16. At this age the stigmas of the disease are already deeply imprinted, and the age of optimum response to treatment has probably passed.

The age factor in relation to the institution of treatment has varied greatly in the series under consideration. Patients have shown a beneficial response to the injection of gonadotropic hormones from the age of 3 years[7] to 40 years. The latter concerns a recently recorded case by Sexton.[17] He reported descent of the testes in a man of that age with double cryptorchidism. Treatment with pregnancy urine extracts succeeded after all other forms of therapy had failed. Most observers conclude that the response to treatment is more marked during the age when puberty may normally be expected to occur. Wangensteen[26] believes that undescended testes show degenerative changes after the age of puberty. Pace and Cabot[27] state that certain retained testes possess the ability to develop as late as the fifth decade. The studies of Moore[23] have shown that the germinal epithelium deteriorates in the retained testis, although the interstitial tissue is relatively unaffected. Evidence that the interstitial cells of the retained testis are capable of functioning under the influence of gonadotropic hormones is shown by the careful studies of Nelson[28] in rats rendered experimentally cryptorchid. The seminal vesicles and prostates which showed an absence of the effect of testicular hormone in these cryptorchid rats before treatment were normal after injection of gonadotropic extract. The effect of gonadotropic hormones on the production of testicular hormones in hypogonadal patients is now in the process of study in our laboratory.

In regard to descended but hypoplastic testes, Moore[23] has shown that the testes are damaged only when removed from the scrotum into the higher temperature of the abdomen. This would suggest that the normally placed hypoplastic testes would not show the degeneration of the cryptorchid testes, and that lack of function of the anterior portion of the pituitary gland is the chief defect in such patients. Although many factors other than dosage and length of treatment probably influence the results obtained, figures indicate that undoubtedly many failures are due to insufficient dosage. We believe that this is par-

ticularly true in the treatment of patients past the age of normal adolescence. Six hundred r.u. weekly is probably the minimum effective dose, and 1,000 r.u. is more nearly optimum in such individuals. The opinion is prevalent among physicians that these older patients have little or no hope for the correction of their condition, and as a result treatment is often half-hearted. It is true that the results are less satisfactory, but the literature reveals 7 patients who were successfully treated after the age of 18. All of them received at least 1,000 r.u. per week, and in several, much larger doses were employed. In these older patients doses as large as 2,000 r.u. per week are indicated for the best results. In all patients it is well, however, to start with the small doses and increase until a change is noted. This is especially true in young children.

It appears advisable to start with a dose of 100 r.u. every other day, and gradually to increase this dose without altering the interval until either a satisfactory response is noted or the limit of tolerance is reached. This final dosage should then be maintained until development is normal for the patient's age. When this has been accomplished, treatment should be discontinued and the patient observed at intervals. Too rapid development should be avoided. Relatively few remissions are noted in the literature. In all types of underdevelopment, treatment should be continued intensively for at least 3 months before failure is admitted. Testes which could not be found on careful examination have been caused to appear in the canals and descend into the scrotum.[10]

Present-day gonadotropic extracts are practically non-toxic, even in large doses, and in most instances cause only a little discomfort at the site of injection, or occasionally slight malaise. A few untoward effects have been reported. Aberle and Jenkins[7] noted nausea and vomiting in 2 patients and were forced to discontinue treatment in 1 patient because of too severe reaction. In 1 case a precocious development of the genitalia in a boy of 3 was noted. Dorff[10] noted slight traces of albuminuria in a few patients. These reactions occurred with the older extracts. With the new, more purified preparations few ill effects have been reported. Goldman et al.[14] report a reaction in a boy of 11 years with bilateral cryptorchidism, who received massive doses of 250 to 750 r.u. three times a day. The testes were swollen and painful; the leukocyte count rose to 23,000 and the temperature to 103°F. with severe chills. Koplin[29] noted hyperglycemia and glycosuria in 1 case, but there are no other instances confirming this observation.

Before the injections are begun the patients should be carefully questioned about allergic symptoms, and if the history is at all suggestive, an intradermal test for sensitivity to the solution to be employed should be made before use. This applies especially to extracts made directly from the anterior pituitaries of animals, but the precaution should not be omitted even when pregnancy urine extracts are employed.

CONCLUSIONS

1. From a study of the literature, we have been able to collect 122 cases of cryptorchidism or sexual hypoplasia in which the results of treatment are described sufficiently for analysis.

2. These patients can be divided into three groups: (1) unilateral cryptorchidism; (2) bilateral cryptorchidism; and (3) hypoplastic testes in the normal scrotal position.

3. In unilateral cryptorchidism the mechanical factors are more important and the endocrine element less definite than in the other two groups.

4. The results of treatment were regarded as successful in 50 per cent of the unilateral cryptorchid cases, in 72 per cent of the bilateral cryptorchid cases and in 73 per cent of the eunuchoid group. The significance of these figures is discussed.

5. Success with the hormone therapy of these conditions depends more upon the intensity of treatment than upon the total amount administered. It is advisable to give at least 600 r.u. weekly to every patient who can tolerate that amount and from 1,000 to 2,000 r.u. weekly to the more resistant individuals.

6. If optimum functional results are to be obtained, treatment should be instituted well before the age of puberty, and not delayed until failure of spontaneous correction has been finally demonstrated.

7. The possibility of allergic reactions to pituitary extracts must not be overlooked.

8. Physiologically standardized preparations should be employed.

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MATERNAL AND CHILD-HEALTH AND CRIPPLED CHILDREN'S PROGRAMS UNDER THE SOCIAL SECURITY ACT

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THE Social Security Act authorizes appropriations for the purpose of enabling each state to extend and improve (especially in rural areas and in areas suffering from severe economic distress) services for promoting the health of mothers and children and services for crippled children. The annual appropriations are $3,800,000 for maternal and child-health services and $2,850,000 for services for crippled children. The major portion of the funds paid to the states to provide maternal and child-health services and all funds for services for crippled children must be matched by the states.

The responsibility for developing plans for the extension of these services, according to the provisions of the act, rests with the official state agencies. The state plan for maternal and child-health services is prepared by the state health agency; that for crippled children by the state agency that is responsible for the medical care of crippled children. State plans for both maternal and child health and crippled children must fulfill the provisions of the Social Security Act as outlined in Title V, Parts 1 and 2, before they can be approved by the chief of the Children's Bureau of the United States Department of Labor.

Further information regarding these federal grants in aid to the states may be found in Maternal and Child Welfare Bulletin No. 1, which is available from the Children's Bureau.

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This bureau is entrusted with the administration of these two services for mothers and children under the Social Security Act. Both the maternal and child-health and the crippled children's divisions are under the direction of physicians and under the general supervision of the assistant chief of the Children's Bureau, who is also a physician.

The field work in the Children's Bureau is carried on by regional medical consultants and public-health nursing consultants. The medical field consultants are available for consultation services to state health officers and to the directors of maternal and child-health and crippled children's programs. They also help with the preparation of state plans and budget forms for submission to the Children's Bureau. The public-health nursing consultants assist in developing the parts of the general public-health nursing program that relate to maternal and child health and crippled children, and will especially emphasize programs for the education of the staff.

Consultants in medical social work, nutrition, obstetrics and orthopedics will assist in these phases of the maternal and child-health and crippled children's programs.

The maternal and child-health portion of the act enables each state to provide adequate state administrative and consultant services and local health services to communities where assistance is most needed. In the furtherance of a state-wide maternal and child-health program, it is essential first to establish a division of maternal and child

health in the state health department in order to provide the leadership and administrative assistance necessary to develop local services. This division should be directed by a full-time, qualified medical director, who is responsible to the state health officer.

Before the beginning of the social security program, only thirty-one states had divisions of maternal and child health in the state health departments, and in only twenty-two of these states were there full-time medical directors of the divisions. At present all the states have a division or bureau of maternal and child health, and all but two states have appointed a medical director of the division. Most of the recently appointed directors of maternal and child health are pediatricians or obstetricians, or physicians with training in both pediatrics and obstetrics, and in a few cases, training in public-health administration as well.

Public-health nursing activities in state health departments are usually administered through a separate unit under the direction of a supervising nurse. This division is usually a major one in the department, and the director is responsible to the state health officer.

The function of the division of maternal and child health is primarily advisory and educational. The program develops along the lines of (1) statewide educational programs for both lay and professional groups, and (2) assistance in local services.

The needs of local communities of course vary enormously. In large parts of many states, and in certain areas in nearly all states, there are communities that have no maternal or child-health services. In such communities everything must start from scratch, but under the social security program the state health agency helps them to make a beginning in meeting their needs.

The sums appropriated under the act are not intended to provide all the necessary services to communities but to enable the states to extend their own services, especially in rural areas. A state may select an area that is in great need of assistance and establish a demonstration service in maternal and child health there during the year, with the expectation that the community will gradually take over the program and ultimately release these state and federal funds for use in another community.

Under the Social Security Act many different programs have been worked out by the various states. The plans vary according to the needs in the state and also according to the child-health services that are now being conducted there. In practically all the states, however, the aim is to make certain minimal health facilities available to mothers and children who would otherwise be unable to obtain them.

The educational programs in the state plans are organized along the following lines:

(1) Education of the staff, which means provision for the additional training of workers in the state health departments and for those engaged in local health work in order that they may give more adequate service to mothers and children.

(2) Postgraduate courses for local general practitioners in order to bring to them current knowledge in the fields of pediatrics and obstetrics and its practical application to maternal and child-health supervision. Many state and local medical societies, in co-operation with state health departments, have already organized such courses under the social security program.

(3) Instruction in maternal and child health for the general public, given chiefly by means of talks, exhibits, classes and the distribution of literature.

(4) Student education, given through such courses as child care and personal hygiene for school children.

(5) Parent education, given through the distribution of literature, health talks, classes, health teaching and demonstrations at prenatal and child-health conferences, and individual instruction given by public-health nurses when they visit the homes.

Local health services for mothers and children will naturally depend upon what is already being done in the different localities of a state. In some areas where there is at present no public-health nursing, a public-health nursing program is being established; in other parts of the state where there is no school program for the physical examination and the follow-up of school children, this is being developed in conjunction with a general service for mothers and children.

In some states the program for maternal and child health includes a dental program under the direction of a full-time or part-time dentist, and in some instances dental hygienists are included.

Other states are planning a nutrition program, and others are promoting a special project for the care of prematurely born infants. On the staff of some state health departments a practicing obstetrician has been appointed to further especially the program for maternal welfare. Many states, in conjunction with the maternal-welfare committee of the state medical society, are investigating maternal deaths and existing facilities for maternal care, and are considering ways and means of improving and extending such care.

For a good maternal and child-health program in a state, it is desirable to have technical advisory committees, composed of members of medical, nursing and dental societies, meet with the offi-

cial state agency in order to confer on the different phases of the program. Many state medical societies have appointed such committees, which have been most helpful in developing programs in co-operation with state health departments.

In addition to technical committees, most of the states have appointed a general advisory committee composed of representatives from allied groups. The appointment of such committees is in accordance with the sixth requirement of Title V, Part 1, of the Social Security Act, which is "provision for co-operation with medical, nursing and welfare groups and organizations."

In the crippled-children's program, the aim is to give every crippled child in need of care such services as will enable him to be put in the best possible physical condition and will help him find his place for service in the world's work.

Existing programs in the states vary widely in the quantity and quality of services for crippled children. It is not expected that these programs will develop according to a uniform pattern. Each state must necessarily be guided by its own needs and conditions. Some states have need of more orthopedic surgeons, while others have an inadequate number of hospital beds for orthopedic patients. Some states have many children in need of treatment on the waiting list for hospital care—even of 2 to 3 years' standing; frequently, as the result of such delay in carrying out the recommendations of an orthopedic surgeon, the child needs a more extensive operation than would have been necessary if treatment had been instituted when he was first examined. Some states are not able to provide adequate follow-up services, such as nursing and social service; thus, in many instances, a child has had to undergo additional surgical treatment because his brace was not properly attended to at home or because his parents failed to co-operate when it was time for the child to return to the hospital.

The Social Security Act should help to bring into public view some of the needs of crippled children that are now overlooked, or for which the states are unable to make adequate provision. In drawing up plans in the several states the aim is to supplement the work now being done, but in no way to duplicate it. Activities under the act will not relieve any state agency, local community or private organization of any responsibility in regard to services for crippled children, but will rather add to this responsibility when these services are increased and extended.

In many areas, children with physical handicaps are likely to be left without the corrective care that might restore them to normal childhood. Very unequal provision—and in many states very inadequate provision—is made for the care of crippled children. We believe that there is a large group of children who are in need of diagnostic services, medical and surgical treatment, and convalescent care. The actual number of children needing this care is not definitely known, but recent state-wide surveys give definite information that a large number living in rural areas and small towns will be forced to go through life with severe handicaps unless public funds are made available for their care.

What is the most effective and most economical way to bring the greatest good to the greatest number of handicapped children in need of care? All of us who are interested in crippled children are bending our united efforts to help answer this question. The answer will of course vary according to the local needs in each state, but within the framework of national, state, local and private participation the answer can and ultimately will, we hope, be found.

When we are planning this well-rounded program for crippled children, we should not only be concerned with the health and welfare problem but should also consider what facilities are available for education. Adequate education is of great importance in the life of a crippled child, in order to make him feel that there is a place for him in the school system, where he can be given work that he can perform with satisfaction and success, and where he can be helped to face life unafraid of his handicap and able to mingle with his fellows on a give-and-take basis.

In addition to providing the so-called "formal education," the citizens of a state who are interested in the problem of the crippled child should ask themselves these questions:

(1) What is being done in my state to train such children in vocational pursuits?

(2) When they have been sufficiently trained, are there opportunities open to them to carry on their trades or to find places in industry?

(3) What assistance are state employment facilities and sources giving?

(4) Is the state itself making efforts to find places for such persons in its own organization, or are we simply reconstructing bodies and training minds and hands and then not helping the individuals to find their places for service in the world's work?

The success of all the work for crippled children depends on a co-operative undertaking among official state agencies, such as departments of welfare, health, education and vocational training. It depends also on the co-operation and help of doctors, nurses, clinics, hospitals, social workers and private organizations. It is also necessary

that there be a public appreciation of the standards of service that must be maintained in the states in order that the contemplated benefits may be made really effective in the lives of children. For the proper functioning of a good program for the care of crippled children, it is most essential to have professional advisory committees on the technical phases of the work. Such a committee might well be composed of orthopedic surgeons, pediatricians, public-health nurses especially trained in orthopedic nursing, and social service workers. This committee should serve in an active advisory capacity, meeting regularly with the official state groups.

The Children's Bureau has followed this procedure; it has a general advisory committee on maternal and child-health and welfare services, and a special technical committee on each of the two divisions of the program—maternal and child-health services and services for crippled children. Other special committees will meet from time to time, such as a committee on maternal welfare, one on training of personnel for the crippled-children's program, and one on hospitals for crippled children. The success of the Social Security Act will depend on combined local, state and federal efforts in developing well-rounded state programs, which means adequate participation by local committees, qualified personnel to carry on the programs, and the interest and co-operation of medical, nursing and social welfare groups.

REPORT OF SEVENTEEN CONSECUTIVE CASES OF FRACTURE OF THE FEMORAL NECK TREATED BY INTERNAL FIXATION

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THE following 17 cases of fracture of the femoral neck are briefly reported, not because they are in any way remarkable, but because they add to the rapidly accumulating evidence of the value of internal fixation.

The Smith-Petersen nail has been used in all cases except one in which wires were used because of necessity (Figs. 1 and 2). In the opinion of the writer, the Smith-Petersen nail, because of its sound and simple mechanical principles, because of its strength, because of its control of rotation of the proximal fragment and because it causes a minimum amount of bone destruction, is the instrument of choice. Other substitutes, wires, pins, and so forth, are necessary in certain cases, but in general they are not so reliable and efficient as the Smith-Petersen nail.

Internal fixation is valuable not only because it promises the best functional results, but also because of economic and other reasons. The comfort of the patient is guaranteed immediately following the nailing of the fracture, which is certainly worth going through with, even though the probability of the patient's survival is dubious. The nursing care is so simplified that it can easily be carried on by the untrained with comfort and safety to the patient. If for economic reasons a short period of hospitalization is necessary, the patient can be moved home almost immediately after the hip is nailed.

The technic used is similar to that described by O'Meara (*J. Bone & Joint Surg.* **17**: 928 [Oct.] 1935), each step being checked by lateral and anteroposterior radiographs. No guiding wire was used in any of the cases.

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CASE REPORTS

Case 1. E. M., a 70-year-old woman, fell in her home, sustaining a fracture of the neck of the femur and a Colles fracture of the left radius. She was taken to the hospital on March 31, 1935. Her general condition was rather poor. She had a high blood pressure but seemed fairly well mentally. On April 1, 1935, the fractured wrist was reduced and the left hip was nailed with a Smith-Petersen nail. Ether anesthesia was used. She made a good recovery from the anesthetic and for about 4 weeks was very comfortable, with free motion of the hip without discomfort. She then rather suddenly developed spasticity of the left arm and became confused. From then on her general condition became worse and on June 11, 1935, she was taken home by her family and died soon after.

Case 2. E. P., a 54-year-old woman, fell on September 2, 1935, and was treated for rheumatism until October 19, 1935, when x-ray disclosed a fracture of the neck of the femur. She also had an ankylosed knee on the same side. Her femur was nailed on October 22, 1935. She was discharged from the hospital on November 24, 1935, walking with crutches. X-rays taken in May, 1936, showed union. No check-up has been made since.

Case 3. N. C., a 50-year-old man, fell off a truck, fracturing the neck of the femur, on November 6, 1935. The femur was nailed November 7, 1935. He was discharged from the hospital January 23, 1936, walking with crutches. He returned to light construction work 2 months later. X-rays taken on September 5, 1936, showed the fracture line still visible with no callus. He is still doing light work and has no symptoms.

Case 4. H. C., an 82-year-old man, fell on April 17, 1936, as he was trying to avoid being struck by an auto-

mobile. The neck of the femur was fractured. He had severe diabetes and advanced progressive muscular atrophy. The femur was nailed April 18, 1936. He walked with crutches after 3 months. Delay in walking was due to general weakness. His hip was painless and active motion was normal. X-rays taken on January 4, 1937, showed callus formation through the fracture line.

Case 5. M. R., an 83-year-old woman, fell on a carpet and fractured the neck of the femur. She was admitted to the hospital April 30, 1936. The femur was nailed May 8, 1936. The operation was delayed because of her poor condition, due to heart disease and arteriosclerosis. She died June 7, 1936, following a gradual decline. There was no discomfort traceable to her injured hip during her last days.

Case 6. A. T., a 61-year-old woman, turned her ankle getting off a trolley car and sustained a fracture of the neck of the right femur. She had an ankylosis of the knee on the same side as the fracture, and this leg was 6 cm. shorter with an equinus deformity of the foot, this being the result of an old infection in childhood. She had a positive blood Hinton test. On May 28, 1936, the femur was nailed, and she was discharged 4 weeks later, walking with crutches. On March 17, 1937, a check-up x-ray was impossible to obtain, but the patient reported that she was able to get about with no symptoms from her hip, and that she felt exactly the same as she did before the fracture.

Case 7. Miss R., a 70-year-old woman, fell on the stairs June 13, 1936, and fractured the neck of the left femur. The femur was nailed June 18, 1936. She was discharged from the hospital August 14, 1936. X-rays at the end of 5 months showed apparent solid bony union, and the patient was walking with crutches. On March 1, 1937, the patient reported that she was as active as usual and without symptoms.

Case 8. N. H., a 65-year-old woman, was admitted to the hospital June 14, 1936, with a fracture of the neck of the right femur. Two weeks previously the patient had fallen; a diagnosis of dislocated hip was made at that time and the hip was supposedly reduced. The femur was nailed on June 26, 1936, and she was discharged July 17, 1936. She was walking with crutches by August 1, 1936. This case was complicated by diabetes. On March 16, 1937, this patient refused a check-up x-ray. Examination of the hip showed it to be stable with a 6 mm. shortening. The hip was painless, but she complained of some stiffness as she started motion and had a noticeable limp. She felt that she had obtained a very good result and was as active as she was before the fracture. An x-ray would probably show some necrosis of the head or proliferative arthritis.

Case 9. A. H., a 58-year-old woman, fell on the floor sustaining a fracture of the neck of the left femur. The femur was nailed August 27, 1936, and on October 5, 1936, she was discharged from the hospital, walking with crutches. Her condition was complicated by cholecystitis, which did not require operation. On January 20, 1937, x-ray showed apparent bony union, and she was walking without crutches. On March 17, 1937, she reported that she was doing her own housework and had no symptoms of any sort from her hip.

Case 10. F. S., a 72-year-old woman, fell while getting out of bed September 4, 1936. Although she seemed fairly well mentally, she had hypertension and was considered a poor risk. Her femur was nailed September 5, 1936, and on September 16 she returned home. She gradually failed and died 6 weeks later. In this case the nailing was of value because it allowed the patient to return home, and to be efficiently cared for by practical nurses.

FIG. 1. Mrs. S., before reduction (Case 16).

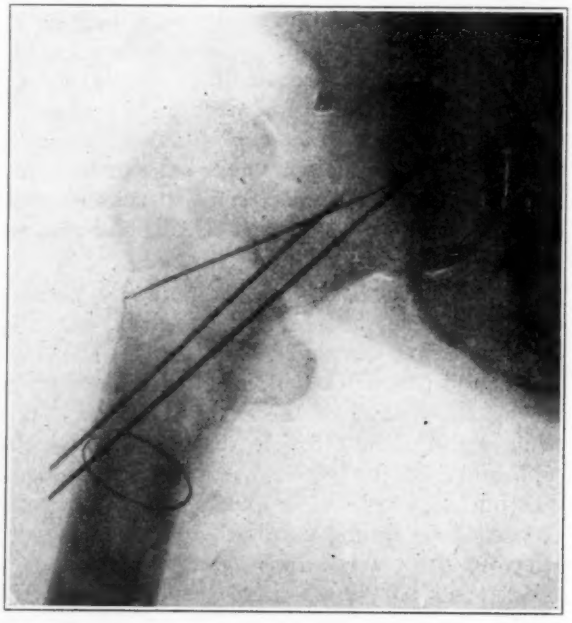

FIG. 2. Mrs. S., after reduction (Case 16).

Case 11. G. A., an 83-year-old man, fell October 27, 1936, and sustained a fracture of the neck of the femur, which was nailed October 28, 1936. Two days later he was put on constant drainage, due to an enlarged prostate. He was very comfortable, and a prostate operation was planned. On December 16, 1936, he had a heart attack, and an aneurism of the aorta was discovered. From that time on he went downhill, and died January 17, 1937.

Case 12. A. T., a 40-year-old man, was admitted to the hospital November 12, 1936, following a fall from a truck. This resulted in a fracture of the neck of the femur, which was nailed November 14, 1936, and the patient was discharged home by ambulance on November 20, 1936. He was up and about with crutches at the end of 6 weeks. X-rays taken on February 25, 1937, showed apparent solid bony union of the fracture. They also suggested a beginning aseptic necrosis of the head.

Case 13. L. S., a 67-year-old woman, fell in a department store December 9, 1936, and fractured the neck of the left femur. On December 14, 1936, the femur was nailed, a local anesthetic being used. This method of anesthesia was chosen because the patient had advanced pulmonary tuberculosis. The operation was carried out with no complaints of pain, and she was discharged home by ambulance December 23, 1936. This patient was extremely emaciated, and following discharge developed a decubitus. She was walking with crutches at the end of 6 weeks. The case has not been checked by x-ray, but she is reported to be walking about and is without symptoms.

Case 14. Mrs. W., a 77-year-old woman, fell in a doorway on December 25, 1936, sustaining a fracture of the neck of the left femur. She was taken to the hospital and Buck's extension was applied. Her general condition was fairly good and on December 31, 1936, the hip was nailed. She made a good convalescence and was about to be allowed out of bed when, on January 13, 1937, she developed bronchopneumonia. On February 2, 1937, she was out of bed, and she was discharged on February 6, 1937. X-rays taken on that date showed some beginning callus formation. She has not been heard from since.

Case 15. Mrs. J. J., a 50-year-old woman, fell on December 9, 1936, sustaining a fracture of the neck of the left femur. She was placed in abduction, and x-rays taken 2 days later showed rather poor position. The patient was exceedingly uncomfortable, consequently on December 16, 1936, the femur was nailed. On February 5, 1937, she was up and about with crutches, and x-rays at that time showed some union. Since that time there has been no report.

Case 16. Mrs. S., a 52-year-old, very obese woman, fell on the stairs July 20, 1936, sustaining a fracture of the neck of the femur and a comminuted fracture through the trochanters of the left femur (Fig. 1). She was treated for 6 weeks with traction by means of a Kirschner wire through the femoral condyles. At the end of 6 weeks

FIG. 3. Typical appearance of hip after being nailed. In this case the nail is slightly lower than is considered ideal.

there was no union and so Kirschner wires were inserted, as shown in Figure 2. At the end of 8 weeks the patient was walking with crutches. On March 1, 1937, she apparently had good union and was able to get about and do her housework.

Case 17. E. H., a 74-year-old man, fell while pruning a tree on February 18, 1937, sustaining a fracture of the right neck of the femur. An anesthetic seemed contraindicated until February 23, 1937, when his heart and general condition had improved. The hip was nailed. He made a good recovery from the anesthetic, and was comfortable from then on so far as his hip was concerned. Ten days after the nailing he developed a pain in his chest, with rusty sputum and other signs of an acute bronchitis. Two weeks later he had recovered from the chest condition and was allowed up in a wheel chair.

20 Maple Street.

HEREDITARY OVALOCYTOSIS (HUMAN ELLIPTICAL ERYTHROCYTES) OBSERVATIONS ON TEN CASES IN ONE FAMILY

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BOSTON

THE occurrence of oval or elliptical erythrocytes in significant numbers in the circulating blood of human subjects, which was first observed by Dresbach[1] in 1904, has been reported in at least 112 individuals since that time.[2–21] The hereditary nature of this condition was suspected by Dresbach and was established by Hunter and Adams.[8] Although the cells were clearly differentiated from sickle-cells by Huck and Bigelow[4] in 1923, the two conditions have not infrequently been confused.[17, 22]

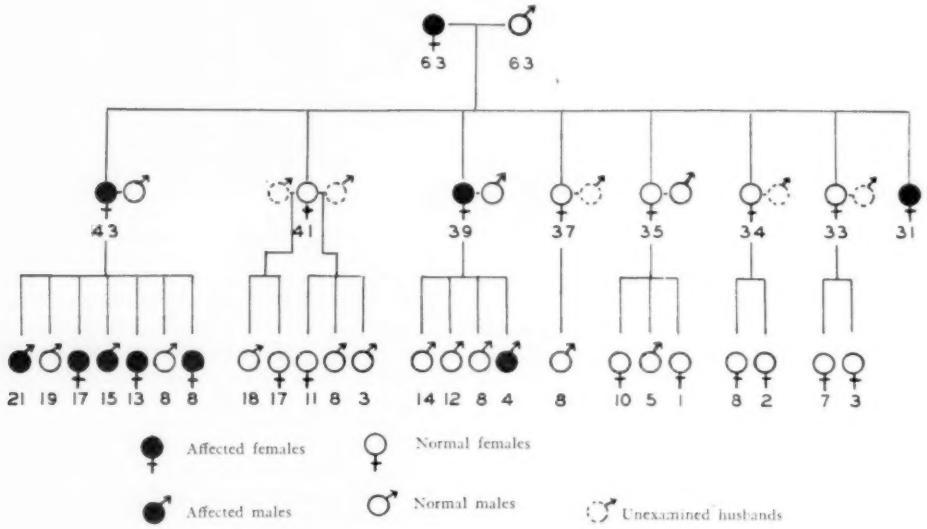

FIG. 1. The inheritance of ovalocytosis. The numbers indicate the ages of the subjects.

The inheritance and morphology of ovalocytosis, as observed by a study of every member of a family of thirty-six individuals, ten of whom had this trait, will be recorded in this paper, together with certain observations on the physiology of oval erythrocytes. Necropsy findings in one of these individuals who had oval erythrocytes and who died of an unrelated condition are also given.

INHERITANCE

The age and sex of the 36 members of this family are shown in Figure 1. Both the husband and the wife of the first generation were born in Russia, of Jewish stock. All the other members of the family were born in Boston. A careful study of the histories of the various individuals failed to reveal any relevant or significant data. None had ever been known to be either anemic or jaundiced. Five of the eight daughters of the second generation had no evidence of ovalocytosis, nor did any of their thirteen children reveal this trait. The other three daughters all showed oval cells, as did six of their eleven children. It is thus apparent that only individuals who have this trait can transmit it and, further, that they transmit it to approximately 50 per cent of their offspring. There is no sex linkage. The trait, therefore, behaves strictly as a mendelian dominant, unit character.

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MORPHOLOGIC OBSERVATIONS

The appearance of the red blood cells in ovalocytosis is essentially the same, both in fresh and in fixed preparations. The essential characteristics are easily observed in the photomicrographic reproductions of blood films, colored by Wright's stain, which were obtained from four different members of the family (Fig. 2). As this figure shows, there is considerable variation in the degree of ovalocytosis in the different members of the family showing this trait. Cell diameters

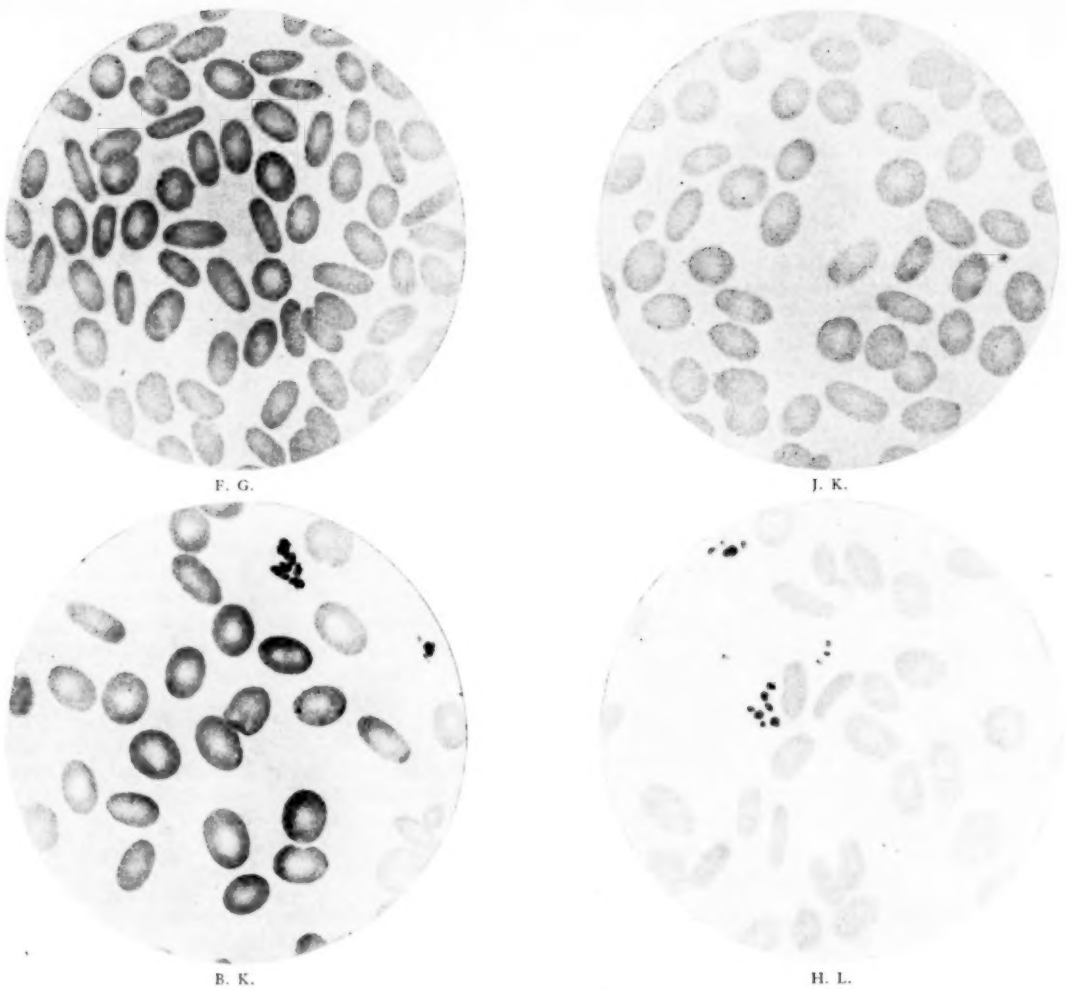

FIG. 2. Photomicrographs of blood films from four affected members of family. Wright's stain.

were measured by the projection method of Price-Jones[23] on 500 cells from each of five normal subjects and from each of the ten affected members of this family. The ten individuals with ovalocytosis showed a difference between the long and short diameters of 2.5 micra or more in 27.6 to 61.0 per cent of the cells, as contrasted with 3.2 to 8.2 per cent in the five normal individuals (Table 1).

Enumeration of the erythrocytes and determinations of the hemoglobin, mean corpuscular volume, hemoglobin concentration and hemoglobin content were normal in two members of this family (Table 2), while the abnormalities on the third member (H. L.) were subsequent to a severe rectal hemorrhage. This patient had an elevated reticulocyte count, which was of particular interest because the reticulocytes were generally round in contrast to the adult cells, 73.6 per cent of which were oval. Those reticulocytes which were not entirely round were only slightly elliptical in shape.

PHYSIOLOGIC OBSERVATIONS

Fresh, wet preparations of blood from subjects with oval cells showed essentially the same percentage of oval cells as did fixed films. Washed oval red cells were resuspended in normal saline solution, in 2.5 per cent sodium citrate solution, in their own serum, in their own plasma, in normal serum and in normal plasma. No detectable change in cell shape occurred. Washed normal red cells were resuspended in the serum obtained from subjects with ovalocytosis. None of the normal cells showed any tendency to become oval.

The red cell resistance to hypotonic salt solution in two of the subjects with ovalocytosis, as shown in Table 2, is essentially normal. In the third subject, H. L., the decreased resistance may have been due to the recent acute blood loss.[24]

Specimens of fresh, sealed preparations of blood from the ten subjects with ovalocytosis, when incubated at 37°C. from 24 to 72 hours, produced no increase in the number of oval cells, in contradis-

tinction to the increase in the numbers of sickle cells which occurs under these conditions in the blood of individuals with the sickle-cell trait.

CASE REPORT AND NECROPSY

The female progenitor of this family, H. L., aged 63, had enjoyed good health until she sustained a fractured hip in an automobile accident, which ultimately led to her death. Her past history revealed that she had had a mastectomy for a benign breast tumor at the age of 46 and had been operated upon for uterine fibroids at the age of 53.

She was seen in consultation with Dr. Otto J. Hermann 6 weeks after the accident and on the day following a very severe rectal hemorrhage arising from a polyp of the colon. Physical examination revealed marked loss of weight, a fracture of the neck of the right femur, scars of a left mastectomy and a laparotomy, generalized arteriosclerosis, prolapse of the uterus and pallor. Laboratory studies other than those of the blood were normal. Four days later a second severe rectal hemorrhage occurred. Five hundred cubic centimeters of citrated blood from a compatible donor was transfused at this time, and again 48 hours later. The patient showed marked clinical improvement for a short time, but then developed increasing mental confusion and unwillingness to eat. Ten weeks after the accident and a month after our first observations, fever of 103°F., tachycardia and leukocytosis occurred. Examination at this time revealed small, clean, decubitus ulcers over the sacrum and right heel and a moderate number of leukocytes in the urine. Death occurred 24 hours after the rise in temperature.

TABLE 1. *Study of Erythrocyte Diameters in Ten Cases of Ovalocytosis Contrasted with Five Normal Subjects*

Name	Mean Cell Diameter in Micra			Long Diameter of Longest Cell in Micra	Long Diameter of Shortest Cell in Micra	Percentage of Cells Showing Difference Between Long and Short Diameters	
	Long Diameter	Short Diameter	Difference Between Long and Short Diameter			2 μ or more	2.5 μ or more
			Cases of Ovalocytosis				
H. L.	8.69	5.70	2.87	11.5	6.0	73.6	61.0
B. K.	8.04	6.29	1.75	10.5	5.5	48.4	30.6
F. G.	8.53	6.03	2.47	11.5	6.0	66.2	51.6
S. G.	7.90	5.92	1.98	11.0	6.0	58.6	36.6
J. K.	8.00	5.42	2.66	10.5	5.5	75.2	60.6
S. K.	7.60	5.65	1.96	10.0	5.5	53.0	37.4
N. K.	8.04	5.70	2.35	11.0	5.0	70.0	53.8
M. K.	7.76	6.00	1.76	11.0	6.0	47.2	29.6
R. K.	7.89	6.20	1.68	10.5	5.0	46.2	27.6
I. G.	7.72	5.62	2.11	10.0	5.5	60.8	42.2
			Normals				
W. C.	7.80	6.83	0.96	11.5	5.5	13.4	4.6
C. H.	7.50	6.68	0.84	9.0	5.5	10.2	3.2
G. D.	7.29	6.60	1.12	9.5	6.0	18.0	8.2
L. Z.	7.52	6.80	0.99	9.5	6.0	14.6	5.6
G. D.	7.48	6.30	1.15	9.5	5.5	20.6	6.8

Necropsy performed 3 hours after death showed a poorly nourished but well-developed woman weighing 99 lb. and measuring 154 cm. in length. Small, clean, decubitus ulcers were noted over the sacrum and on the inner aspect of the right heel. The right leg was 4 cm. shorter than the left. Numerous varicose veins were present over both legs. On opening the abdomen, it was noted that the sigmoid colon was redundant and dilated to a diameter of 10 to 11 cm. In the descending colon near the splenic flexure there was a small, gray, smooth, benign polyp 0.5 cm. in diameter. The spleen was enlarged, weighing 400 gm. The capsule was smooth and of slate color. The cut surface was fairly firm and deep purplish red. The follicles were small, gray in color and easily visible. A small amount of pasty, deep-red material could be scraped from the cut surface. The bladder mucosa was edematous, red and diffusely injected. This was most marked in the trigonal region. The lungs were normal. The heart weighed 390 gm. and showed a few atheromatous plaques on the mitral leaflets and in the coronary arteries. The latter, however, were widely patent. The aorta showed scattered atheromatous plaques. The brain weighed 1,080 gm. The vessels at the base of the brain showed atheromatous plaques and slight narrowing. The meninges were diffusely edematous, light gray in color and less than normally translucent. The bone marrow from the vertebral column, the ribs and the sternum was deep red in color.

The gross anatomic diagnoses were: fracture of the neck of the right femur; arteriosclerosis of the aorta and of the coronary and cerebral arteries; edema of the pia arachnoid; dilatation of the sigmoid colon; benign polyp of the descending colon; cystitis; splenomegaly; varicose veins, both legs; decubitus ulcers, sacrum and right heel.

Microscopic examination showed increased hemosiderin in the liver cells. The splenic sinuses were filled with

TABLE 2. *Blood Values and Erythrocyte Resistance to Hypotonic Saline in Three Patients with Ovalocytosis.*

Name	Date	Red Blood Cells (millions per cu. mm.)	Hemoglobin (per cent) 15.6 gm. = 100 per cent	Hematocrit (per cent)	Mean Corpuscular Volume (cu. micra)	Mean Corpuscular Hemoglobin Content (per cent)	Mean Corpuscular Hemoglobin (micromicrograms)	Icterus Index	Red Cell Hemolysis (per cent of sodium chloride)			
									Trace	Definite	Partial	Complete
B. K.	2-17-36	4.57	82	36.3	79.4	35.2	28.0	5	0.46	0.44	0.30	0.24
F. G.	2-17-36	4.09	83	37.8	92.5	33.8	31.7	5	0.48	0.46	0.34	0.30
H. L.	2-12-36	2.30	41	19.5	84.8	32.8	27.8	—	—	—	—	—
H. L.	2-13-36	2.44	41	18.4	75.4	36.5	27.5	—	0.50	0.48	0.40	0.34
H. L.	3-13-36	3.68	71	34.2	92.9	32.3	30.1	5	0.52	0.50	0.38	0.32

blood. There were many polymorphonuclear leukocytes and pigment-bearing macrophages present throughout the splenic pulp. The kidneys showed a few focal cortical scars with hyaline glomeruli, atrophy of the tubules and infiltration of lymphocytes; there were a few small retention cysts. The bone marrow from the vertebral column, the sternum and the ribs showed increased activity of both the red and the white cell series. There were many adult polymorphonuclear leukocytes scattered throughout, and some scattered macrophages contained blood pigment. There was no apparent abnormality in size or shape of any of the nucleated cells of the red blood cell series.

DISCUSSION

The condition of oval human erythrocytes has not infrequently been confused with the sickle-cell trait or sickle-cell anemia.[17, 22] In contradistinction to the sickle-cell phenomenon, ovalocytosis has never been reported as the cause of anemia or jaundice. Ovalocytosis has been found chiefly in the white race, whereas the sickle-cell trait occurs almost entirely (99 per cent of cases) in the colored race. Incubation increases the degree of the sickling phenomenon but has no effect on oval cells. Heart murmurs associated with long-continued anemia and not due to organic heart disease, which are common in sickle-cell anemia, do not occur in ovalocytosis, since this condition does not lead to anemia, nor are leg ulcers or abdominal crises encountered. These differences indicate that the two conditions, although they are associated with morphologic peculiarities of the erythrocytes, which bear superficial mutual resemblance, may be considered as entirely separate entities.

It is of interest that all three of the important familial erythrocyte abnormalities—spherocytosis (congenital hemolytic icterus), drepanocytosis (sickle-cell trait or sickle-cell anemia) and ovalocytosis—are inherited as mendelian dominant, unit characters.

The fact, also observed by Schartum-Hansen,[19] that none of the nucleated erythrocytes in the bone marrow sections are elliptical in shape, together with the observation that few of the reticulocytes in the preparations of peripheral blood are elliptical, and then only in lesser degree than the adult cells, indicates that the oval shape is completely assumed only after the extrusion of the nucleus and the disappearance of the reticulum.

CONCLUSIONS

1. Ovalocytosis is a condition of human erythrocytes that is characterized by an abnormality of cell shape, which is inherited as a mendelian dominant, unit character.

2. The peculiarity is inherent in the erythrocyte itself and is not affected by washing the cells in saline solution, by resuspending them in normal plasma or by incubation.

3. The resistance of oval erythrocytes to hypotonic salt solution does not differ from that of normal erythrocytes.

4. The condition produces no symptoms or disability of any kind.

5. Ovalocytosis is entirely distinct from and has no features in common with sickle-cell anemia or the sickle-cell trait.

6. The oval shape of the erythrocyte is assumed after the extrusion of the nucleus and is only fully developed after the disappearance of the reticulum.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTEMORTEM AND POSTMORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT, M.D.

TRACY B. MALLORY, M.D., *Editor*

CASE 23281

PRESENTATION OF CASE

A 62-year-old American carpenter was admitted complaining of inability to walk.

About 1½ years before entry, while climbing a ladder, the patient suddenly noted pain in the left foot, radiating up the leg to the hip. A physician stated that he had a strain of the left ankle, and flat feet. The ankles were strapped, and he was given an arch support, which gave him relief. About 7 months before entry, following a long automobile trip, he noted marked weakness of the left knee. This subsided, however, without treatment. Five months before entry he developed pain in the lower back and in the left leg. Strapping and massage produced no relief, and 2 months later he entered the Out Patient Department. Examination there showed that he had a flat, stiff back and that there was pain on bending the back and straight leg raising. An x-ray taken of the lumbar spine showed marked deformity of the body of the fourth lumbar vertebra and narrowing of the disk between this vertebra and the third. There were extensive proliferative changes about the bodies of the fourth vertebra. The body of the second lumbar vertebra showed areas of increased radiability, proliferative changes about its anterior border, and slight narrowing of the disk between it and the first. The lumbar arch was flattened. There was no soft tissue mass or calcification in the soft tissues. He was measured for a belt, but before it was available he was compelled to use crutches because of numbness and weakness of the left leg. The numbness extended down the lateral aspect of the thigh and leg and involved the entire foot. He was given a back brace about a week before admission, but this afforded no improvement. Three days before coming to the hospital he developed weakness in the right knee and fell. Subsequently he was unable to walk at all.

Thirty-five years before coming to the hospital he fell from the roof of a house and remained unconscious for 3 or 4 days and was in bed for 2 weeks. Subsequently he had no further symptoms. Ten years later he had a similar fall and had pain in the left flank for about 2 weeks. Five years before entry he fell from a scaffold for a distance of 25 ft. and injured his back. He was unable to stand at that time, but was able to move his lower extremities. He remained in bed for 8 weeks and was then given a supporting belt, which permitted him to return to work. Subsequently he had no further symptoms until the onset of his present illness.

Physical examination showed a well-developed and nourished man in no acute discomfort. The patient was unable to stand without holding onto a supporting object, but he could sit up in bed. There appeared to be generalized weakness of the legs. There were no definite areas of tenderness, but there seemed to be generalized hypesthesia over the entire lower back. The spine from the middorsal region to the sacrum lacked the normal curve and was stiff, and all motions were limited, although there was no definite muscle spasm. Straight leg-raising was limited on the right to within 20° of a right angle and on the left to within 40°. All hip motions were normal. Passive flexion of the thigh upon the chest produced pain extending down the left leg. Abdominal and cremasteric reflexes were present on the right but absent on the left. Knee jerks and ankle jerks were bilaterally absent. The Babinski sign was negative, and there was no clonus. There was no marked difference in the circumferences of the calves and thighs. Pinprick perception on both legs and the back was essentially unimpaired. There was local tenderness over the entire lower back which was not centered in any single point.

The temperature, pulse and respirations were normal.

Examination of the urine showed a specific gravity of 1.028, and was otherwise negative. The blood showed a red cell count of 4,100,000, with a hemoglobin of 90 per cent. The white cell count was 6,000, 62 per cent polymorphonuclears. A blood Hinton test was negative. A lumbar puncture was done with needles between the fourth and fifth and between the second and third lumbar vertebrae. Fluid from the lower needle was light yellow, that from the upper essentially clear. Pressure at the lower level was 200 mm. of water, and at the upper 210; compression on the jugulars produced a rise at the lower level to 240 and at the upper to 310. Release of the jugulars permitted the pressure to return to 210 on both sides. Fluid removed from the lower needle contained 1,380 mg. per cent of protein, that from the upper needle 126 mg. per cent.

X-ray examination following the instillation of lipiodol into the lower dorsal region showed interruption of the lipiodol at the level of the first lumbar vertebra, with the formation of a slightly

irregular cap. Dilated veins were visible above this area.

On the ninth hospital day an operation was performed.

Differential Diagnosis

Dr. Sumner M. Roberts: The first question is, Was the pain in his left ankle 1½ years before entry related to the present illness? I do not believe so. As a rule pain radiates away from its source. Back pain might radiate to the ankle. It might skip to the ankle without radiation, but I do not think it would skip to the ankle and run back again. Furthermore, simple treatment apparently was effective.

His automobile trip may have some connection with his present complaint. There is nothing harder on a weak back than an automobile ride, unless possibly a good sneeze. The weakness of the knee which followed the auto trip may have been weakness of the whole leg. Weakness is often centered around the knee joint, because that is the point where a weak leg buckles.

Physical examination in the Out Patient Department suggested nothing more than a low back strain. His x-rays, however, did show a good deal: first, deformity of the fourth lumbar vertebra; secondly, narrow intervertebral disks between the first and second and the third and fourth; and thirdly, marked proliferative changes. All three findings can be explained on the basis of past injuries. He had had three severe falls, two from a roof and one from a scaffold 25 ft. high, and I think that any or all of these could have left some mark. X-rays in addition showed deformity of the fourth lumbar vertebra. We do not know the nature of the deformity. Possibly it was a compression fracture, and this again would tend to obliterate the normal lumbar lordosis. There were areas of increased radiability in the second lumbar vertebra, but we do not know just what they were like. That may be the "nigger in the wood pile," and we will keep it in mind.

The physical examination points almost entirely to the lumbar spine as the source of this man's trouble. I would expect him to have more muscle spasm and more definite localized tenderness. It says that there was local tenderness over the entire low back; I do not call that *local* tenderness. Perhaps this physical examination was done a few days after he came into the hospital, after rest in bed, and he had quieted down. That is often the case, and sometimes the house officer's examination when the patient first comes in is more valuable than one done by the visiting man a few days later. The note of the difference in straight leg-raising is not of any importance. It was a good deal better on both sides than many of us here could do. He had pain running down the left leg, presumably posteriorly. That is not enough to implicate a sacroiliac joint. Finally, and most important of all, he had weakness of both legs, with loss of reflexes.

To summarize, we have a hard working man 62 years old, with pain in the back, radiating down the leg, and with progressive weakness of the legs. He has had several accidents in the past, and x-ray showed deformity of the lumbar spine. We have, therefore, some condition in the spine causing pain in the back and leg, and also cord symptoms.

Before going farther let us consider some of the differential points. I think we can rule out any infectious process, such as tuberculosis or osteomyelitis. This man was generally well. The temperature and pulse were normal. The white count was normal, and so was the red count.

Could his symptoms be due to any injury? Not to any bony injury. Compression fractures sometimes cause delayed cord symptoms because of overgrowth of scar and callous tissue, but such symptoms ought to come on sooner than 5 years. The longest interval I have seen has been 1 year. Could his symptoms be due to injury to the intervertebral disk? That is our latest neuro-orthopedic discovery, and our knowledge is still incomplete. We look for disks at the present time a good deal more often than we find them. The history of injury is compatible with this diagnosis, so is the pain radiating down the leg. Both legs were affected, which is somewhat against a disk lesion but does not rule it out. The thing that rules it out in my mind is the rapid increase in symptoms. Disk lesions are usually rather chronic. Three months ago this man had pain and now he is unable to walk. This leaves some sort of disease either in the cord or near by. I do not know which it is. Probably the x-ray will give a clue.

Certainly the x-ray findings make us content with the diagnosis of tumor. The difference in the protein findings means that the levels of lumbar puncture included the tumor site between them. The higher needle however was below the second lumbar vertebra. If that is true this vertebra which we suspected before is out of the picture.

The formation of a cap with the lipiodol is again compatible with a diagnosis of a tumor, but the level is somewhat higher than the lumbar puncture would lead us to believe. I think we will have to assume that the upper lumbar puncture needle was actually one space higher than was recorded. I cannot go any farther than to say that I think there is a tumor, either within the cord or close to it, which presses upon it and is the cause of this man's symptoms.

Dr. Aubrey O. Hampton: The x-ray descrip-

tion of the second lumbar vertebra is not complete. This change in the anterior half of the body is more than diminished density, it is actual bone destruction. It is irregular and extends into the left lamina and pedicle. It is the picture of a malignant tumor in the bone without a surrounding soft tissue mass. This fracture of the fourth lumbar body is just the ordinary compression fracture that has been present for a long time and is now bridged over with bone.

The lipiodol demonstrated a typical block above the diseased vertebra. The process apparently extends upward into the canal, but it does not involve the vertebra above it. It does not cross the joint on either side.

Dr. Roberts: Dr. Hampton has localized the site of this tumor as not being within the cord but outside and involving it. What is the nature of the tumor? It does not look to me like a hemangioma. I have seen a few of them and x-ray pictures of others. I do not see the definite lines or parallel vertical striations which are often present in that type of tumor. I should think that probably the best diagnosis in a man who evidently is not suffering from generalized malignant disease would be some sort of lymphosarcoma. This is one of their common sites, and the patient's age is compatible. I would like to ask Dr. Hampton one question. Does this suggest in any way a disk lesion?

Dr. Hampton: No; it lies between the two disks here, opposite the center of the vertebral body instead of opposite a disk. It does not show the characteristic defect we usually see opposite the lamina. It is above the lamina. I do not know how one could be absolutely positive from this lipiodol examination that it was not intrinsic in the cord, though the finding of the disease in the vertebra is strong inferential evidence that the lesion is extrinsic. I saw the films before I knew the diagnosis and I thought that someone had gone over to the Baker and picked up one of my films. The picture presented on the film is very striking; although I am afraid we have not made it apparent from the description. I have not seen such a picture in anything except chordoma, although it does suggest hemangioma, but, as you say, the striations are not vertical. Also, in hemangioma, the anterior body is involved; here the anterior one-fourth of the body is not involved, and this queer destruction of the pedicle and lamina would also be rather unusual.

Dr. W. Jason Mixter: It seems to me that there is a definite error in the record. Whoever did the lumbar puncture certainly got in above the tumor, and miscounted. Dr. Roberts accepted the third lumbar vertebra as the level, but I do not think it could have been there. With a total protein of 1,300 mg. per cent below and 126 above, his upper needle must have been above the lesion, and with as good a cap formation as there is, we cannot doubt that the lesion is at the level of the first lumbar vertebra. So there is a definite, misleading error in the record which bothered us at the time that we operated on this patient. As Dr. Hampton says, he and I had been familiar with a case at the Baker that we had studied for a long time and that had exactly the same type of bone defect, so perhaps we had a bit of a lead over the rest of the x-ray department.

The tumor did involve the spinal canal, and there was a large opening extending down into the center of the vertebra.

Dr. Tracy B. Mallory: Do you want to describe the rest of your operation, Dr. Mixter?

Dr. Mixter: This is the kind of case one should remember. It is very unusual. The tumor was bluish-brown in color and extended into the spinal canal through a rather definite opening in the dura. It did not lie simply anterior to the dura, but had broken through it, so that there was a finger of tumor extending into the spinal canal and almost obliterating it. The nerve roots overlay the tumor mass. After the intraspinal portion was removed, the cavity could be followed down, and the whole center of the body of the vertebra could be scraped out with a blunt curet. That was done, leaving a very thin shell of bone around most of the cavity, but practically no bone at all on the left side. Dr. Mark Rogers then took over the operation and did a spinal fusion.

Preoperative Diagnosis

Chordoma.

Dr. Sumner M. Roberts's Diagnosis

Primary malignant tumor of the second lumbar vertebra (lymphosarcoma ?).

Anatomic Diagnosis

Chordoma of the second lumbar vertebra.

Pathological Discussion

Dr. Mallory: The gelatinous material which was removed from this case showed microscopically the characteristic picture of a chordoma, the rather rare, peculiar tumor which is presumed to arise from congenital rests of the notochord which persist up and down the spinal column in a significant number of individuals but which lead to tumor formation very infrequently, except at either end of the neural canal. This tumor was higher in the vertebral column than is usual. It would be much more common to find it involving the sacrum itself.

Dr. Mixter: I think this is the second case in

this hospital which was in the lumbar or dorsal region.

DR. MALLORY: The tumors are infiltrating, hence locally malignant. In general they do not metastasize, but a small number of cases with metastasis are on record. The tumors usually are slowly growing and on that basis Dr. Mixter called the orthopedist to do a spinal fusion.

DR. MIXTER: Our next step will be x-ray therapy, with which in a recent case we had excellent results.

DR. HAMPTON: Chordoma is said not to be radiosensitive, but the only one I have treated was. This was a sacral case, where a tumor the size of a grapefruit disappeared under very heavy radiation.

CASE 23282

PRESENTATION OF CASE

A 59-year-old retired American fireman was admitted complaining of jaundice.

The patient had been perfectly well until 4 months before entry, when he noticed loss of energy and ready fatigability. There was progressive anorexia and rapid loss of weight. Three months before admission he noted that his urine had become quite dark and his stools pale yellow in color. At about the same time jaundice appeared and increased rapidly in intensity. Bowel movements increased from the usual single movement daily to two to three times a day. Two months prior to admission, because of intense itching of the skin, the patient was admitted to a hospital, where he remained for 4 weeks. During this time several x-ray studies were made, and all were reported negative. Four weeks before entering this hospital the jaundice became slightly less intense and the stools, which had become clay-colored, exhibited a yellowish tint. The itching became less severe, but anorexia and weight loss continued. During the 4-week period preceding entry the stools showed gradual but slight increase in color. There were no chills, fever, night sweats or attacks of pain.

Physical examination showed a well-developed but poorly nourished, moderately jaundiced man, lying comfortably in bed. There were numerous scratch marks on the skin of the body. The sclerae were icteric. The pupils were negative. Examination of the fundi showed slight beading of the retinal vessels. The heart was normal. The blood pressure was 110/75. The lungs were clear. The abdomen was soft, and there was no tenderness. The edge of the liver was sharp and smooth and extended three fingerbreadths beneath the costal margin. No other abdominal masses were palpated, although one examiner stated that there was a vague mass in the epigastrium just to the right of the midline. The mass was said to be firm and to move with respiration. Rectal examination was negative.

The temperature, pulse and respirations were normal.

Examination of the urine showed a specific gravity of 1.022. There were a trace of albumin and a moderate amount of bile present. The sediment contained 3 to 5 white blood cells and an occasional hyaline cast per high power field. The blood showed a red cell count of 3,000,000, with a hemoglobin of 80 per cent. The white cell count was 12,500, 76 per cent polymorphonuclears. The stools were light brown in color and of seven specimens examined at scattered intervals three gave 1+ reactions to the guaiac test; the remainder were negative. The nonprotein nitrogen of the blood serum was 42 mg. per cent, the plasma protein 4 gm. per cent, and the van den Bergh showed 8.13 mg. per cent of bilirubin with a direct reaction. The Takata-Ara test was positive. The blood clotting time was 8 min.

An x-ray film of the chest showed an old, calcified, tuberculous process in the left apex, but the lung fields were otherwise clear. The heart was not remarkable. The intervertebral space between the fourth and fifth lumbar vertebrae was markedly decreased, and there was deformity of the fourth lumbar vertebra, with scoliosis to the left in this region. There was calcification of the abdominal aorta. A gastrointestinal series showed a large liver shadow. The esophagus was normal. The stomach was slightly displaced to the left, and the duodenal cap showed a pressure defect near its tip. In the upright position it was possible to bring only a small amount of barium into the duodenum, and in the horizontal position the duodenum was obscured by the barium-filled colon. A re-examination of the duodenum showed the pressure defect at the beginning of the descending duodenum, but the remainder of the intestine in this region was negative. A lateral film of the lumbar spine at this time showed an abnormality in the region of the fourth and fifth lumbar vertebrae, which was partially obscured by the barium-filled colon. It was impossible to determine whether this was an old fracture or spondylolisthesis.

The patient's condition gradually improved and the van den Bergh diminished to 6.9 mg. per cent. On the twentieth hospital day a laparotomy was performed.

DIFFERENTIAL DIAGNOSIS

DR. ALFRED O. LUDWIG: This sounds on first reading like the usual story of painless jaundice in a man of 59. His loss of energy and ready fatigability could mean the onset of almost any

disease process, but progressive anorexia and rapid loss of weight are perhaps somewhat more suggestive of a malignant growth. Apparently there was some disturbance in the physiology of the gastrointestinal tract soon after the onset of his jaundice, and this may be explained most simply, perhaps, by the absence of bile from the stools and consequent disturbance of digestion of fats and proteins. According to the story there was a remission in the intensity of the jaundice. This is usually a very unreliable story coming from the patient alone, but in this case we know that the stools, which had been clay-colored, became yellow, and this seems very good evidence that actually there had been a remission of the complete biliary obstruction that was present during the time when his stools were clay-colored.

Physical examination does not help us very much. The fact that the liver was palpable three fingers beneath the costal margin does not indicate more to me than the increase in size of this organ that one would expect with long-continued obstruction to the outflow of bile. No mention is made of any masses in the liver; so that we are unable to say that metastases are present, since it is only possible to say that masses in the liver are due to secondary metastases if they are large enough to be felt by abdominal palpation. Mention is made of a vague mass in the epigastrium just to the right of the midline, but this is notoriously a difficult area to palpate due to the presence of segments of the rectus muscle, and observations such as this one are frequently incorrect.

Examination of the urine does not tell us more than that this man had severe jaundice with bile being excreted through his kidneys. I am not entirely certain, but I think that the trace of albumin is perhaps best explained on the basis of biliuria alone. The specific gravity of 1.022 pretty well rules out any serious involvement of the kidney, such as a chronic nephritis. The blood findings are consistent with a diagnosis of malignancy, or might be secondary to a nutritional deficiency, since there was anorexia over a period of 4 months. Apparently during his stay in the hospital, bile was present in the stools. I am inclined to disregard the 1+ guaiac reactions which were found on three out of seven occasions, although it might be possible to speculate that the presence of this severe degree of jaundice may have caused some slight oozing of blood from the intestinal walls. The nonprotein nitrogen of 42 mg. per cent is definitely above the limits of normal, but I think in this instance our best explanation is dehydration, although there are no facts in the history to substantiate this. The plasma protein of 4 gm. per cent is also probably due to his lack of sufficient intake of food, particularly of protein, since the onset of his illness. The van den Bergh of 8.13 mg. per cent is definitely abnormal, the normal figures being 0.5 to 1 mg. I am not inclined to place much importance on the fact that this is a direct reaction, as we have come to lay more stress on the quantitative aspects of the test in this hospital than on the character of the reaction.

The next fact mentioned is that the Takata-Ara test was positive. The Takata-Ara test in well-marked cases of cirrhosis of the liver in which there is no doubt about the diagnosis from the clinical point of view is positive in about 70 per cent, but usually it is of very little help in cases where cirrhosis of the liver is suspected but where the clinical picture is not conclusive. It might be an indication in this case of a secondary biliary cirrhosis resulting from obstruction to the biliary outflow and possibly also due to some secondary infection. I do not feel that the story up to this point gives us any lead pointing to a diagnosis of portal cirrhosis.

The blood clotting time of 8 min. is within the normal range. This was probably done because it was felt that this man would come to surgery and that consequently it would be important to establish any abnormality of his bleeding and clotting time. As a matter of fact, postoperative bleeding in cases of severe jaundice does not seem to be very closely related to bleeding and clotting time. Such bleeding may occur in the presence of normal figures for both tests.

I do not believe that the x-rays of the chest are of importance in this case. They show an old, calcified, tuberculous process, which apparently is of no consequence whatever at the present time. The abnormality in the fourth and fifth lumbar vertebrae might make us think of metastatic lesions with secondary fracture, but according to the interpretation on the sheet this also is an old process, and I do not believe it helps us very much in establishing a diagnosis. The pressure defect occurring in the duodenum, which is mentioned in the report of the gastrointestinal series, I am not able to explain satisfactorily. Possibly this is due to pressure of a large gall bladder, or more likely due to old adhesions from previous pathology in and around the gall bladder. One wonders whether the pressure defect might possibly be caused by a tumor in an adjacent organ, perhaps the head of the pancreas; but I cannot be sure of this.

During his course in the hospital we again note diminution in the patient's jaundice, and there can be absolutely no doubt about it here, because it was established by a decrease in the van den Bergh reaction from 8.13 mg. to 6.9 mg.

So far as differential diagnosis in this case is

concerned, it is my impression that it falls between a stone in the common duct and carcinoma of the head of the pancreas. I do not believe that we are dealing with a cirrhosis. The only type of cirrhosis of the liver that could give this picture and this degree of jaundice would be a biliary cirrhosis, of which there are two types. The first is primary biliary cirrhosis, which is an exceedingly rare condition. I believe only one case of so-called Hanot's cirrhosis has been reported from the pathological laboratory here. Furthermore, this condition is usually associated with an extremely large liver, which is not present in this case. The other type is so-called secondary biliary cirrhosis, which follows obstruction or infection of the common or hepatic bile ducts. Undoubtedly there is some secondary biliary cirrhosis present here, as one would expect following any sort of obstruction; but this obviously will not explain the nature and the cause of the obstruction which primarily interests us.

Could this man have had a catarrhal jaundice which went on into a subacute yellow atrophy? I do not believe that the findings that we have in the history and physical examination are at all those which one sees in this condition. Furthermore, one would expect that after 4 months the liver, instead of being large, would be definitely decreased in size.

As to the diagnosis of stone, of course most of the clinical features of stone in the common duct are not present in this case; there is no history of pain, of nausea or vomiting, of previous indigestion, or of previous attacks of colic. These facts, however, certainly do not rule out the possibility that this man's obstruction is due to stone, as we have seen cases with a very similar story when the diagnosis of common duct obstruction by stone has been established by laparotomy after everyone had felt preoperatively that the diagnosis was malignancy at the head of the pancreas. When the diagnosis between these two conditions is not clear, and when the patient is in good enough condition, a laparotomy should be done and the diagnosis established, as a so-called silent stone is a not infrequent occurrence.

One of the things that seems very incongruous in this study, especially for the diagnosis of carcinoma of the head of the pancreas, is that this man's jaundice decreased. I have never seen a case of proved carcinoma at the head of the pancreas in which this has taken place, and it is very hard to conceive of an obstruction due to tumor of this sort being relieved other than by some bizarre and unusual happening such as ulceration with sinus formation between the gall bladder and the bowel. If this had taken place there would almost certainly have been some signs of peritoneal irritation with pain, fever and the like, and these are entirely missing. With stone, however, one not infrequently sees a temporary relief in a complete obstruction, and it is perfectly feasible to suppose that a stone lodged in the ampulla might slip out and slip back to allow obstruction to be released and to recur. I do not believe that I can go any farther than this, and I will say that the diagnosis lies between stone in the common duct and carcinoma at the head of the pancreas. I favor the former diagnosis, but would not be surprised to find that this man had carcinoma at the head of the pancreas at operation.

X-Ray Interpretation

Dr. Richard Schatzki: The upper part of the descending duodenum shows the pressure defect described. It is consistent with that produced by the neck of an enlarged gall bladder. Below this defect a slight irregularity was noticed on the medial aspect of the descending duodenum, which did not seem to be very constant during the examination, but which now, after knowing the correct diagnosis, seems to be very definite. There is an area of rigidity about 3 cm. in diameter along the medial aspect of the descending duodenum just where it joins the third portion of the duodenum. On one of the films there is a crater visible in the center of this area creating the impression of a centrally ulcerated lesion, which protrudes into the duodenum from its medial aspect.

Clinical Diagnosis (Preoperative)

Carcinoma of the head of the pancreas.

Dr. Alfred O. Ludwig's Diagnosis

Stone in the common bile duct?
Carcinoma of the head of the pancreas?

Anatomic Diagnoses

Adenocarcinoma of the papilla of Vater.
Duodenal ulcer, old, perforated and sutured.
Operation wounds: cholecystenterostomy, suture of perforated peptic ulcer.
Peritonitis, acute, generalized, *Streptococcus hemolyticus.*
Obstructive biliary cirrhosis.
Jaundice.
Empyema, left, *Streptococcus hemolyticus.*
Arteriosclerosis, moderate, generalized.

Pathological Discussion

Dr. Benjamin Castleman: At operation the surgeon found the stomach quite adherent to the liver at a point just proximal to the pylorus. As this was freed an old perforated, pyloric ulcer was uncovered and was sutured. The gall bladder was markedly distended and filled with greenish

bile. The entire pancreas felt very nodular and although the surgeon was not at all certain whether it was neoplastic, in view of the history of jaundice he performed a cholecystenterostomy. The patient did poorly postoperatively and died on the fourth day.

The autopsy explained quite well the symptoms that seemed to Dr. Ludwig somewhat incongruous with his diagnoses. In the region of the papilla of Vater was an ulcerated tumor about 3 by 1.5 by 0.2 cm. which at the time of autopsy had produced complete obstruction to the flow of bile. The intermittent character of the jaundice, which is so frequent in common duct stones, is also one of the cardinal symptoms of cancer at the papilla of Vater and is due either to the secondary necrosis of the tumor with subsequent release of the obstruction of the common bile duct or, if the tumor is polypoid in nature, to a ball-valve action on the lumen. The latter is naturally more common with tumors within the papilla than with those arising on the duodenal surface of the papilla. The sections showed a well-differentiated adenocarcinoma. The presence of occult blood in the stools has been pointed to as a helpful clue in making this diagnosis, but positive guaiacs are so common with all forms of jaundice that one could not place much weight upon it.

The duct of Santorini was patent and opened into the duodenum, 1 cm. above the tumor. The old perforated peptic ulcer turned out to be on the duodenal side of the pylorus and was well sutured. The liver was somewhat enlarged, weighing 2,000 gm., and microscopically showed early obstructive biliary cirrhosis. The immediate causes of death were a peritonitis and left empyema due to a hemolytic streptococcus.

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APPROACHING THE FIFTY YEAR MARK

One of the very last acts of the late Dr. Cousens, president of Tufts College, was to endorse and forward the enterprise of its medical alumni in launching a campaign for the beginning of a long-term program of improvement intended to include buildings, equipment and instruction.

An institution that can outlive those who founded it has demonstrated its worthiness. Its achievements must have comprised something more than the guiles of whoever happened to develop the original promotive power. The power itself must have had more than a social or financial background for Tufts College Medical School to approach its fiftieth anniversary in apparent health and with more men from New England among its students than any other school. One quarter of the membership of the Massachusetts Medical Society is composed of Tufts graduates.

Thus there are a large number of doctors who will be interested in the development of this attempt to meet the rapidly changing standards of the day. There is no plan to enlarge classes or to enter new fields; the improvements sought are relatively no greater than those in every other walk of specialized activity—professional or commercial. Nor is this any more a day of change than is called for by our constantly shifting environment. The news item in this issue is the natural expression of a current of medical evolution which is in keeping with the times. The *Journal* wishes Tufts College Medical School all success.

MEDICAL SERVICE TO THE INDIGENT

Two communications to the House of Delegates of the American Medical Association at the recent annual meeting at Atlantic City and the action relating to them concern important questions before the medical profession.

The President of the United States, through his representative, Senator J. Hamilton Lewis, requested that the American Medical Association should co-operate with federal agencies in the development of plans to give medical care to those unable to pay for it, with the information that impending legislation will deal with this matter. Whether the President's purpose is confined to hospitalization of the indigent or includes domiciliary service does not appear in the published reports. After the delivery of the President's message, the senator, speaking for himself, stated in substance that he is a proponent of social security legislation and that he favors suitable control of medical service to the indigent and methods of payment incident thereto.

In the course of his address he expressed appreciation of the high standards of American medicine and of plans underway for meeting the needs of the poor with the proviso that there should be freedom from political control, but he warned the profession that there must be an adjustment of its attitude to changing conditions under way and that doctors engaged in carrying out plans for serving the indigent must realize that they are "officials" of the government.

The President's communication was referred to the trustees of the association. An exact definition of the meaning of the senator's remarks relating to changing conditions existing and impending and the status of physicians employed by the federal government would enable the profession to approach more intelligently the problems that wili

be submitted in the conferences to which doctors will be invited.

It may be difficult to convince persons somewhat familiar with the purposes of the average office-holder in dealing with matters of public concern that it will be possible to keep appointments of officials out of political control. If in the future the selection of executives in departments of public service is based on merit, the millennium is near at hand. However honest one may be in such matters, history shows that politics enter into nearly every phase of public service; hence, even these assertions of the honorable senator cannot, without further assurances, dispel uncertainty in the minds of physicians as to the position of federal employees.

Any plan devised for dealing with this matter must have the approval of the medical profession. Unfortunately the lay mind rarely seems to understand fully the principles underlying medicine in its relation to the physician and patient.

The other matter was presented by delegates of the New York State Medical Society as an appeal for action on the proposition that public funds should be available for meeting the cost of medical care for those too poor to pay for it. These matters were considered by a reference committee with the result that no direct reply to the resolution submitted by the New York delegation resulted. The adopted committee report reads as follows:

> Your reference committee recommends that the bureaus, councils and committees of the Association continue their studies of the need for and the methods of distributing medical care to the end that the American Medical Association shall continue to do everything possible to promote and protect the health of the American people.
>
> The American Medical Association reaffirms its willingness, on receipt of direct request, to co-operate with any governmental or other qualified agency, and to make available the information, observations and results of investigation, together with any facilities.

It would have been courteous to have incorporated some explanation of the omission of reference to the New York society's proposition because of the large membership of this society and its representation by seventeen delegates. The sentiment expressed in the proposition has been a subject of discussion and justifies the expression of the attitude of organized medicine. It is not strange that some resentment was expressed in the published reports of the meeting, for the burden carried by the profession in its service to the poor is worthy of adjustment in so far as physicians have been expected to relieve communities of an expense which should be met as a common responsibility. We may expect that, even though the wish of the New York society for action has been sidetracked, further discussion will result in the formulation of a policy that will be given general endorsement.

ATTORNEY GENERAL OPPOSES CORPORATE PRACTICE OF PROFESSIONS

Attorney General Paul A. Dever, in his report to the General Court of Massachusetts for the year ending November 30, 1936, calls particular attention to the practice of the professions by incorporated organizations. According to this report, the practice of a profession, such as medicine, dentistry, optometry, and the like, is not a business open to all, but is a personal right limited to persons of good moral character, with special qualifications. As these conditions cannot be fulfilled by corporations or lay persons, he points out, it follows that the practice of a profession is not one in which a corporation should engage. However, various sections of the General Laws (Tercentenary Edition, Chapter 112), permit corporate practices in some professions.

In the light of this interpretation, the attorney general recommends to the General Court that legislation be designed to curb the increasing encroachment of corporate professional practices, and suggests that it might be advisable that the General Court appoint a recess commission to study the subject of exploitation of professions, with power to recommend such proposals as it feels practical in the premises.

Considering the present widespread agitation concerning the gradual encroachment of civic bodies on professional practice, some comfort may be drawn from the attitude of at least one public official who apparently seeks to return professional practice to the professions.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY

M. Fletcher Eades, M.D., *Secretary*,
19 Bay State Road,
Boston, Mass.

Case History No. 28. Miscarriage at Four and One-Half Months. Retained Placenta

Mrs. A. H., a white, American-born housewife, 33 years old, about 4½ months pregnant, tele-

A series of selected case histories by members of the Section will be published weekly.

Comments and questions by subscribers are solicited and will be discussed by members of the Section.

phoned on the evening of October 14, 1936, saying that she thought she had lost some water, and also stating that 3 or 4 days previously she had had a small amount of reddish discharge, which had necessitated her going to bed.

There was no family history of tuberculosis, diabetes, malignancy or hemorrhagic disease. At the age of 6 she had had diphtheria. She also had had malaria, chicken pox, whooping cough and measles. Her tonsils had been cut twice but never thoroughly removed. She had had one full-term child on August 11, 1934, and during this pregnancy a cervical polyp had been removed, when she was about 2½ months pregnant. Her basal metabolic rate had always been low, being minus 25 in March, 1934, and she had been taking 6 gr. of Burroughs-Wellcome thyroid extract daily for some time. Her periods had begun at 11 years of age; they were regular, consistently 30 days apart. Her last period was on June 7.

On examination, she was a well-developed and nourished woman. The mucous membranes were of good color. Her heart and lungs were negative; her lungs were resonant throughout. Her abdomen was negative save for a symmetrical tumor, rising about three fingerbreadths above the symphysis, compatible with a pregnancy of 4½ months' duration. Her breasts were firm, and Montgomery's glands were enlarged. Her extremities were negative. There was no glandular enlargement. Her blood pressure was 120/60. A vaginal examination was not done.

The patient had been seen routinely since August 24. She had had a slight show beginning July 29 and occurring off and on for 3 weeks, during which time she was in bed. At the routine visit on October 5, Mrs. H. reported that she had had a slight reddish discharge about 3 weeks previously and again 10 days previously, lasting for about 2 days.

The patient's blood Wassermann was negative. Her urine showed no abnormalities.

She was sent into the hospital and was told that if she really had lost some water, the chances were that she would miscarry. She was treated 100 per cent conservatively. For 5 days there was only a small amount of discharge. On the fifth day the patient began to flow slightly and had some cramps. The following day the fetus was passed. There was no bleeding, and the placenta was not delivered. The uterus was in no way invaded. The patient's temperature and pulse remained normal. In the absence of bleeding, the placenta was left in situ, with the hope that nature might normally deliver it without artificial interference. However, on October 26, she began to flow somewhat freely and passed some clots, and under gas-oxygen anesthesia, the placenta was manually removed very easily. Her convalescence from then on was quite uneventful, and the patient was discharged 5 days after the placenta was delivered.

Comment. The conservative treatment of miscarriages from 3½ months on cannot be too strongly advocated. The fear of infection developing if the placenta remains in the uterus is greatly exaggerated. There is no indication for invading such a uterus in the absence of bleeding. The removal of a placenta, between the fourth and sixth months, that has not separated is oftentimes a difficult and hazardous performance, associated with a good deal of bleeding and not infrequently with subsequent sepsis. It is always a very good habit to live up to the oft-repeated dictum: "Do not invade the uterus except for hemorrhage."

MISCELLANY

TUFTS COLLEGE MEDICAL SCHOOL CAMPAIGN

Dr. John A. Cousens, president of Tufts College, authorized the announcement, shortly before his untimely death, of plans to raise $2,000,000 by public appeal as the first step in what will ultimately be a $5,000,000 fund for the Tufts College Medical School.

The decision to go to the public of New England for funds was reached at a recent meeting of the Board of Trustees. Preliminary work of the campaign, which is sponsored by the Tufts College Medical Alumni Association, of which Dr. A. K. Paine is president, is already in progress. It will culminate in December. Although Tufts's long-term program contemplates new medical school buildings and other improvements, the $2,000,000 to be sought now will be used to build and equip a surgical unit as part of the New England Medical Center, to create a fund for its maintenance, for additional professorships, and for equipment at the medical school.

"Our problem today is mainly one of man-power," said Dr. A. Warren Stearns, dean of Tufts College Medical School. "It is not our intention to enlarge our classes but rather to turn out graduates better equipped in the practice of modern medicine. Our present teaching staff is inadequate to accomplish this purpose as fully as we would wish. The family doctor is in greater demand than ever before, particularly in the smaller communities of New England, and it is and always has been the aim of Tufts to turn out family doctors who are thoroughly familiar with modern medicine, not only in theory, but in actual practice.

"The clinical facilities of the New England Medical Center are unsurpassed anywhere in the United States. The result is that the man who graduates from Tufts has had a wealth of actual experience both in the clinic and in the patient's home—experience which enables him to meet any problem he is likely to face.

"The standards of medical education in recent years have been greatly improved, but our lack of funds has made it difficult to keep pace with the requirements of modern clinical teaching. So far we have done this by volunteer effort but we must now meet the situation by creating additional professorships and by increasing the remuneration of our present staff in several departments.

"A weak point in the New England Medical Center has been its lack of facilities for following through on surgical cases. The new surgical unit will overcome this defect."

The New England Medical Center, which is composed of three co-operating units,—the Boston Dispensary, the Boston Floating Hospital, the Tufts College Medical School,—serves a threefold function. To the patient without money, or with very limited means, it brings the best possible medical aid; to the practicing physicians, particularly those of rural New England communities, it provides an organization for diagnosis of complex medical problems; for the Tufts College Medical School, which provides more practicing physicians for New England than any other educational agency, it provides teaching facilities, through which much of the third and fourth year work is accomplished.

Recently, a gift of more than $500,000 was announced from William Bingham II of Bethel, Maine, for the creation of the Joseph H. Pratt Diagnostic Hospital. To complete the New England Medical Center group, as well as to make possible improved instruction for Tufts medical students, a surgical unit of from fifty to sixty beds is badly needed.

CONNECTICUT NEWS

Infant Mortality

Connecticut reported the lowest infant mortality among the states for 1936 and New Haven the best record among the 93 cities in the 100,000 and more population group. The infant mortality rate for Connecticut was 42.1.

Health Conservation Contest

The Hartford Board of Health received a certificate for meritorious achievement in the Health Conservation Contest for 1936, sponsored by the United States Chamber of Commerce and the American Public Health Association. In a letter sent by the grading committee of the contest the principal services recommended for improvement were preschool diphtheria immunization, preventive medical services for infants and preschool groups and preventive dental service. The committee particularly commended Hartford for the addition of a laboratory technician, a tavern inspector and a Negro nurse to the Board of Health personnel, for the vigorous campaign by the Hartford Chamber of Commerce to maintain ordinances for qualified health officers, and for the reorganization of the health department. The grading is measured by the community improvement on its own past rather than by comparison with competitors.

Health of Industrial Laborers

Dr. Alice Hamilton, professor-emeritus of industrial hygiene at Harvard Medical School, in an address recently before the Consumers League of Connecticut, named one of the greatest problems now facing industry as that of the health of the worker. Dr. Hamilton devoted most of her address to a relating of the conditions under which women work. She asserted that low wages and the speed with which factories are turning out their products contribute more than anything else to the poor health of women laborers. The problem of fatigue among women workers is caused mainly by this speed which their employers demand. Shortening of working hours seems to be the only way there is of dealing with this health problem. In reply to this the league appointed a special committee to study this problem.

State Department of Health Laboratory Adopts Kline Test

After a study of comparative tests on more than 5,000 specimens, the State Department of Health has adopted the Kline exclusion test as a routine test on all blood specimens for syphilis in the Bureau of Laboratories. The change will apply only to specimens of blood; spinal fluids will be tested as at present. This change will make possible earlier reporting of specimens needing no further study, since the Kline test requires no holding period comparable to that necessary for fixation of complement in the Wassermann test. Hence, in many cases, physicians should receive reports of specimens submitted the same day.

New Southington Hospital

The contract for building the Bradley Memorial Hospital in Southington has been awarded to H. Wales Lines Company of Meriden. Construction started about July 1. The total cost of the building, including mechanical equipment, will be about $115,000.

Facilities of the new hospital, the first of its kind in Connecticut, will be given over for the most part to preventive medicine. Part of the basement and the entire first floor of the two-story L-shaped building will be used for a clinical public health service. The top floor will be used exclusively for emergency hospitalization and will contain a complete, modern operating suite and a hospital outfit for 8 to 10 beds. The basement will have space for an ambulance and other vehicles, boiler room, accident and special treatment rooms, storage, kitchen and quarters for the janitor and his wife. On this same floor will be a venereal disease clinic.

Funds for the institution were left by Mrs. Julia A. Bradley who died February 21, 1919. The will calls for the building of a hospital within 21 years.

Deaths

MERRIAM—Adeline Colt Merriam, M.D., a practicing physician in Hartford for more than 50 years, died on May 28 at the age of 95. Dr. Merriam, the widow of Ezekiel R. Merriam, was born March 5, 1842, in Harwinton, a daughter of Wolcott and Polly Thompkins Colt. Having been engaged in nursing since the age of 15, and always eager to become a doctor, she applied herself studiously in 1881 to medical books and journals. She set herself up in medical practice for a time, until, anticipating the passage of legislation making a medical degree compulsory, she entered Bellevue Medical College in Boston. She graduated from that school with a doctor of medicine degree in 1888, and also was graduated from the College of Therapeutics, Boston, in the same year. Following her graduation Dr. Merriam began to practice in Meriden. At the end of two years she gave up her practice, and in May, 1890, married Ezekiel R. Merriam, of Meriden. The couple moved to Hartford, and Dr. Merriam resumed the practice of medicine, which she continued until two years ago. Her husband died in 1901. She was proud of the fact that during her many years of practice she issued only two death certificates. Dr. Merriam was a charter member of the State Spiritual Association, and spent each summer at her cottage at the association's camp in Niantic. She was the last surviving charter member of the organization. Dr. Merriam also held membership in the National Women's Medical Association. She is survived by a sister, Mrs. Julia A. Judson, of Hawleyville, and several nieces and nephews.

SAVARD — Stricken with a heart attack as he was marching with the American Legion Fife and Drum Corps in the Memorial Day parade, Dr. A. J. Savard, of New Britain, died a few hours later.

Born in Waterbury, he was graduated from Crosby High School and later went to the University of Michigan. He studied medicine at Tufts College Medical School. While at Tufts, the United States entered the World War, and he enlisted in the medical corps, serving 15 months before being discharged. After completing medical school he did postgraduate work at Massachusetts General Hospital, Boston City Hospital, Robert Breck Brigham Hospital, Boston Dispensary and St. Francis Hospital, in Hartford. His family by that time had moved to Bristol, but he chose New Britain as the place to enter practice 18 years ago. For three years he was head of the New Britain Medical Society and for two years he was police surgeon. Interested in Legion affairs, he gave particular attention to the drum corps and is given credit for its rejuvenation during recent years. Moved by his spirit the corps, which had lapsed after earlier triumphs, was planning again this year to resume participation in competition in New York City and elsewhere. For an avocation he took up painting and had several notable works to his credit. He was also fond of archery and was active in the Paquabuck Club.

Dr. Savard was the gynecologist on the staff of the New Britain General Hospital at the time of his death. Beloved among the hospital officials and nurses, his death deeply moved all who had been connected with him in his medical work there. His general practice was unusually large and for years he had been regarded as one of the city's leading physicians. Besides his mother, he leaves his widow, Mrs. Margaret Savard; a son, Dudley; a daughter, Jane; and two brothers, Ernest E. Savard, of Bristol, and Dr. Henry Savard, of Baltimore, Md.

APPOINTMENTS BY THE GOVERNOR

Dr. Marshall L. Alling, of Lowell, was recently reappointed medical examiner of the fifth Middlesex district by Governor Hurley, and Dr. Michael A. Tighe, of Lowell, was appointed associate medical examiner of the same district.

HARVARD PROFESSOR OF PREVENTIVE MEDICINE AND EPIDEMIOLOGY

Dr. John Everett Gordon, of Chicago, field director of the International Health Division of the Rockefeller Foundation, has been appointed professor of preventive medicine and epidemiology at the Harvard Medical School. He will assume his duties in the fall of 1938, taking over the chair made vacant two years ago by the retirement of Dr. Milton J. Rosenau and now temporarily occupied by Col. Frederick F. Russell.

THEOBALD SMITH AWARD IN MEDICAL SCIENCE

Robley D. Evans, of the Massachusetts Institute of Technology, was given the Theobald Smith Award in Medical Science by the American Association for the Advancement of Science at its recent annual meeting. The $1,000 prize, to be awarded annually to a deserving, young investigator in medical science, was given for the first time this year.

The award was based on methods of detecting minute amounts of radon in the blood of persons exposed to radium poisoning and of extracting radium from the bones of poisoned individuals before the disease is fatal.

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR MAY, 1937

Diseases	May, 1937	May, 1936	Five-Year Average*
Anterior Poliomyelitis	1	15	6
Chickenpox	1579	877	1005
Diphtheria	21	24	66
Dog Bite	1238	1237	954
German Measles	259	1043	2237
Gonorrhea	—	441	486
Lobar Pneumonia	434	423	368
Measles	2953	6104	4102
Meningococcus Meningitis	33	27	11
Mumps	747	1889	1061
Scarlet Fever	977	923	1278
Syphilis		446	407
Tuberculosis, Pulmonary	280	339	338
Tuberculosis, Other Forms	25	35	48
Typhoid Fever	4	8	11
Undulant Fever	1	4	3
Whooping Cough	1220	331	736

*Based on figures for preceding five years.

RARE DISEASES

Anterior poliomyelitis was reported from Somerville, 1.

Anthrax was reported from Lynn, 1.

Diphtheria was reported from Boston, 11; Brockton, 2; Danvers, 1; Lowell, 1; Lynn, 1; Malden, 1; New Bedford, 1; Newburyport, 1; Salem, 1; Westwood, 1; total, 21.

Dysentery, amebic was reported from Chelsea, 1.

Dysentery, bacillary was reported from Somerville, 1.

Meningococcus meningitis was reported from Arlington, 1; Boston, 9; Cambridge, 1; Chicopee, 1; Everett, 1; Fall River, 1; Foxboro, 1; Greenfield, 1; Hadley, 1; Leominster, 1; Malden, 1; Medford, 1; Monson, 1; New Bedford, 1; Newton, 1; Northampton, 1; Norwood, 1; Palmer, 2; Quincy, 3; Revere, 1; Wellesley, 1; Worcester, 1; total, 33.

Pellagra was reported from Boston, 1; Pittsfield, 1; total, 2.

Septic sore throat was reported from Andover, 1; Boston, 7; Brookline, 2; East Bridgewater, 5; Fall River, 1; Gardner, 6; Greenfield, 1; Hampden, 1; Rowley, 1; Waltham, 1; total, 26.

Typhoid fever was reported from Boston, 1; Fitchburg, 1; Millbury, 1; Worcester, 1; total, 4.

Undulant fever was reported from Natick, 1.

Paratyphoid B was reported from Billerica, 2; Boston, 3; Burlington, 1; Everett, 1; Lawrence, 9; Lowell, 7; Lynn, 14; Malden, 1; Medford, 2; Melrose, 5; Methuen, 3; Reading, 1; Saugus, 2; Somerville, 1; Stoneham, 5; Wakefield, 3; Winchester, 11; Woburn, 9; Quincy, 1; total, 81.

Typhus fever was reported from Boston, 1.

Diphtheria continued to show record low monthly incidence figures for the eighth consecutive month.

Paratyphoid fever had the highest incidence recorded for any month or year to date. All of the May cases were part of the same outbreak responsible for the April cases. Very few of the May cases were due to secondary infection.

Whooping cough and chicken pox had the highest reported figures for any year to date. The May incidence of chicken pox was the highest ever recorded for that month.

The reported incidences of lobar pneumonia and meningococcus meningitis continued above the five-year average.

Typhoid fever and tuberculosis (other forms) had the

lowest recorded incidences both for May and any year to date.

Pulmonary tuberculosis had the lowest May incidence ever recorded.

Anterior poliomyelitis continued to have the lowest reported incidence for any year to date.

The reported incidences of scarlet fever, mumps, measles and German measles continued to be below the five-year average.

The reported incidence of undulant fever was not remarkable.

The reported incidence of animal rabies was the lowest for May ever recorded except for 1933, which it equaled. The number of cases reported for this year to date exceed that for last year. Foci of animal rabies were most noticeable in the North Metropolitan area, North Shore, Walpole, Norwood, Tewksbury and Middleboro.

CORRESPONDENCE

SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA

To the Editor: As you may well imagine, I have read with considerable interest the article by Frederick C. Waite, Ph.D., entitled "The age of Harvard Medical School in relation to that of other existing medical schools in the United States," which appeared in the March 11 issue of your *Journal*.

Last year, the University of Pennsylvania shared with the mutual pride of all universities of this country in the fact that Harvard had reached the ripe age of three hundred years, full of well-deserved honors and with a record of distinguished service throughout these three centuries.

The University of Pennsylvania has inaugurated active plans for the celebration of its Bicentennial in 1940. We have as a model the splendid Harvard Tercentenary celebration and shall do our best to imitate it. Of course, if many of the contentions set forth in the article by Dr. Waite are correct, then we should not observe this Bicentennial celebration until 1991. Eminent historians who have taken the trouble to study the original legislative acts and other source material have, however, reached the conclusions which we share. Since we believe that these other authorities have construed the original data correctly, we do not agree with the conclusions of Dr. Waite and are, therefore, going ahead with our plans for the celebration.

Dr. Waite early in his article makes the statement that the Medical School of the College of Philadelphia came to an end in 1779 and that the University of the State of Pennsylvania was finally closed in 1791. This is quite incorrect. The School of Medicine of the University of Pennsylvania runs back continuously to 1765. What happened in 1779 is often misunderstood. It was not that the old charter was "abrogated" as Dr. Waite says and as the expression is often used. It was not the charter that was changed. It concerned the men who administered it. The law of 1779 describes itself as "An act to confirm the estate and interests of the College, Academy and Charitable School of the City of Philadelphia and to amend and alter the charter thereof conformably to the Revolution . . . and to erect the same into a University." The old charters of 1753 and 1755 were expressly re-enacted and confirmed, except in a few points, one of which was to alter its name from College to University. The old trustees complained, not that the old charter was abrogated, or the old institution brought to an end, but only that they had personally been disenfranchised and their right to administer it taken away from them. The medical courses like other courses went right on under the changed name and under the new group of trustees.

Edward Potts Cheyney, now the Henry Charles Lea Emeritus Professor of History at the University of Pennsylvania, has given much study to this matter, and in his "History of the University" describes the changes which took place in its early history, citing the official documents which I have above briefly outlined.

In 1789, when the legislature restored to the old group of trustees their property and their right to give degrees, they simply called back their old medical professors and added some new ones. But since the law of 1789 had taken away from the trustees of the University only their property, not their franchises, they also continued their medical courses, and for two years there were two medical schools in Philadelphia, both drawing their powers from the same charter of 1755 and working under the original organization of the medical school of 1765. Dr. Shippen was on both faculties, and the other professors distributed themselves between the two.

The enabling act of 1791, which allowed the two groups to unite, so far from being the end of the two existing schools, as Dr. Waite says, was simply the union of the two, nothing being said of bringing either of them to an end. Dr. Waite's statement that there were in Philadelphia in the eighteenth century "three different medical schools under three different charters" is just a plain misstatement. His recapitulation, where he says the University of the State of Pennsylvania was not the legal successor of the College of Philadelphia and that the University of Pennsylvania was not identical with either or both of the older institutions, is again a misstatement. Dr. Waite quotes from Professor Cheyney's book to the effect that after 1774 "the medical course fell into disuse." This is exactly the same statement that would have to be made concerning every other educational institution in the colonies in those troublous days when the confusions of the Revolution were just coming on. It was as true of the college as it was of the medical school, and as true of other institutions as it was of ours. There exists, therefore, no consternation among the graduates of this medical school subsequent to 1791 about the legality of our degrees for we rest securely on the charter of 1755.

The perpetuation of a quibble in matters of such a character arouses no enthusiastic emotions in the minds of most men of intelligence. I have no desire to prolong this discussion but I realize that it would be distasteful to thoughtful alumni of the Harvard Medical School to allow any inaccuracy of fact and interpretation to detract from the distinction of a sister institution of at least contemporaneous origin. The illustrious past and present of Harvard University would make it seem unnecessary for any one enthusiastic alumnus to "gild the lily."

WILLIAM PEPPER, M.D., *Dean.*

School of Medicine,
University of Pennsylvania.

A copy of this letter was sent to Dr. Waite, who replies:

To the Editor: When the article to which Dr. Pepper refers was written, it was foreseen that there might be disagreement with some of the interpretations there made, and therefore toward the end of the article it was suggested that, in regard to two series of events, two interpretations were possible in each instance, and the reader was given his choice of interpretations. Dr. Pepper does

not distinguish between statements of facts which are documented and interpretations of the author. It would have been more gracious for him to have written *misinterpretation* instead of *misstatement* in two places. Furthermore, he does not recognize that succession of educational efforts by the same or by different groups in one locality is not synonymous with corporate identity.

Dr. Pepper mentions the date 1940 as in some remote way connected with my article. From Professor Cheyney's history one gleans that in 1740 an unroofed building to accommodate a religious revivalist was erected in Philadelphia by public subscription. The funds were secured on the representation that with them would also be established and conducted a primary school for indigent children. No teaching, even of primary grade, was inaugurated, and in 1747 some of the subscribers petitioned the legislature to compel the trustees to refund their contributions or turn over the building, since the educational features upon which solicitation was based had not been carried out.

Two years later a new and incorporated organization bought the building, which had been completed and used for purposes of church and public assembly, and reimbursed the petitioning subscribers. In 1750 a teacher was employed and in 1751 the first pupils were received into an academy. After two years collegiate instruction was begun, and in 1755 a charter empowering the granting of degrees was secured. The first degree was granted in 1757 and it was under this charter that the medical degrees from 1768 to 1774 were conferred.

Whether the solicitation and collection in 1740 of public gifts, part of which were returned to contributors on their complaint that no educational use of them was made, and the selection of trustees of an unchartered organization who did not carry out any of the educational features of their trust, are suitable events for a great modern educational institution, following the conclusions of eminent historians, to choose as its founding, does not pertain to the several auspices under which medical instruction was conducted in Philadelphia beginning twenty-five years after these events.

The act of 1779 came at a time when the College of Philadelphia had been inactive for at least two years and when there was doubt as to the legal qualifications of the majority of its trustees.

By that act all its assets were taken away and conveyed to a corporation of a new name and the former trustees were deprived of all legal status. This terminated for the time being the College of Philadelphia in name. Professor Cheyney designates this act as "remodelling the college."

The College of Philadelphia was an institution supported from private sources. The University of the State of Pennsylvania was a different type of institution supported from public funds, the first American institution to be designated as a state university. The title of the bill was euphemistic and perhaps concealed as well its real purpose as did the reasons given for the change conceal the real reasons for that change.

Objection is made to my use of the word "abrogated." It has been frequently used by previous writers on these events. From 1779 to 1789 the College of Philadelphia was nonexistent in fact, in name and in legal status, and during that period it must have seemed to have been terminated.

Two days before the repeal act of 1789 a committee report was adopted by a large majority in the assembly which, regarding the act of 1779, states: "The act which took away the charter of the College, Academy and Free School of the City of Philadelphia was not founded on any just forfeiture of the said charter." A few days later the provost of the revived college in public notice says, "the schools are now opened on their ancient foundation." This cannot mean as a branch of the University.

In the Laws of Pennsylvania, "republished under the authority of the legislature by Alexander James Dallas," in 1797, the marginal note opposite section 3 of this act of 1779 is: "Former charters and bye-laws declared null and void." Mr. Dallas was at that time secretary of the State of Pennsylvania. The index of this volume says: "The Charter of the College of Philadelphia annuled and its estate transferred to the University of Pennsylvania: the University incorporated and endowed."

The general assembly in 1781 empowered Thomas McKean, then chief justice of Pennsylvania, "to revise, compare, correct, and have published with marginal notes" the Laws of Pennsylvania "now in force." The charter of 1755 is not included. This volume was published in 1782 and certified by Justice McKean. The marginal note of section 3 of the act of 1779 reads "Former charters and bye-laws declared null and void."

The act of 1789 says that the powers, authorities, and so forth, by the act of 1779 were "vested in a new corporation or body politic thereby created and established."

Whatever may be Dr. Pepper's opinion, the chief justice in 1782, the legislators and the provost of 1789, and the legislators and secretary of state in 1797 believed that the charter was abrogated in 1779 and that the University of the State of Pennsylvania was a "new corporation." If the charter of the College of Philadelphia lost its validity in 1779, its medical school must have terminated corporately also. Dr. Pepper says that the act of 1789 "restored to the old group their property and their right to give degrees." Restoration predicates prior annulment.

Since the repeal act of 1789 declared unconstitutional so much of the act of 1779 "as touch, or in any wise concern or relate to said antient institution," that is, the College of Philadelphia, and since the charter and name were the essence of that college, the conclusion seems warranted that this language estopped the University of the State of Pennsylvania from legal succession to either the name or charter of the College of Philadelphia.

If there be any doubt that the University of the State of Pennsylvania was not, immediately after the act of 1779, the same institution as the former College of Philadelphia, that doubt should be dispelled when from 1789 to 1791 the two institutions were operating side by side under different boards. One institution cannot be the same institution as another separate corporation in active existence contemporaneously. The college derived its legal status from the charter of 1755 revived by the act of 1789. The University derived its legal status from the parts of the act of 1779 that were not declared unconstitutional.

Since the act of 1789 declares unconstitutional all parts of the act of 1779 that "concern or relate" to the College of Philadelphia, the University of Pennsylvania cannot derive through the University of the State of Pennsylvania, established by the act of 1779, any identity with the College of Philadelphia. If such identity exists, it comes from the act of 1755 and its revival by the act of 1789, without intervention by the act of 1779.

The act of 1791 establishing the University of Pennsylvania is not entitled an amendment to any previous act. It does not mention the acts of 1755 or 1779, or the corporate rights, powers or privileges of the former insti-

tutions. It mentions funds and property to be united, and persons to be selected, but there is no mention of union of rights, powers or privileges.

Since no instruction was carried on and no degrees were conferred after 1791 under the name of either the College of Philadelphia or that of the University of the State of Pennsylvania, it seems a reasonable interpretation that these institutions under these names ceased, determined and expired as corporate entities as of 1791.

Let us see what an eminent historian says. In 1902 Professor Cheyney published a history of the University of Pennsylvania, four years after it had selected a new and earlier date for its founding. In his interpretation of events he stresses continuity. He denies the validity of the interpretation of earlier writers that the act of 1779 abrogated the act of 1755. Nevertheless he says: ". . . an act was therefore passed on the thirtieth of September, 1791, embodying these proposals and incorporating a new institution, the University of Pennsylvania."

The whole series of events in the early years of this republic concerning the educational institutions of Philadelphia is unique, interesting and complicated. Modern collegiate institutions base the inviolability of their charters on the decision of the United States Supreme Court in 1819 in the Dartmouth College Case, but there is precedent thirty years earlier in the repeal act of 1789 in Pennsylvania, which declared tampering with the charter of an educational institution as "repugnant to justice, a violation of the constitution and dangerous in its precedent to all incorporated bodies."

I have given no intimation that any of the medical degrees granted in Philadelphia were illegal. All were granted under enactments by competent legislative authority, but under three different acts, one supplemented by a fourth act, which repealed unconstitutional features in the second act.

The appeal to sentiment regarding the disasters of the Revolutionary War period, common to many institutions, and to the mutual friendship of two great universities, cannot change the text of several legislative enactments of about a hundred and fifty years ago.

There is no escape from the facts that medical instruction was conducted and degrees were conferred in Philadelphia between 1765 and 1800 by institutions of three different names under three different legislative enactments, or four such counting the repeal act of 1789, and that for a period two of these institutions were in operation coincidentally under different legislative acts and with different boards of trustees.

The publication of these facts does not detract from the glory due the educational forces of Philadelphia in inaugurating the first institutional medical instruction in the present United States and in continuing that instruction under the trying circumstances that pertained to the latter third of the eighteenth century.

My article was not written from the ex parte viewpoint of "one enthusiastic alumnus." Had it been I should have refrained from divulging my discovery that the long-cherished date of 1782 as the founding of the Harvard Medical School is, on the written testimony of the founders themselves, one year too early. The paper is one of a long series of efforts to search out little-known facts concerning early American medical education and then to interpret the relations of those facts.

FREDERICK C. WAITE.

School of Medicine,
Western Reserve University.

VOLTAIRE HAS THE SMALLPOX

To the Editor: The following account is from "Voltaire," by Alfred Noyes, published by Sheed and Ward, New York, 1936.

Noyes tells us that Voltaire had just arrived at the Chateau de Maisons, where he was to read "Mariamme," his tragedy of King Herod, before some thirty guests at the chateau. Late at night he was suddenly taken seriously ill, and the celebrated physician, Gervasi, was sent for from Paris.

Smallpox was diagnosed, and the guests fled in panic. Voltaire says that Gervasi "had a very poor opinion of my case; the servants noticed it, and did not fail to let me know. I made my will, and awaited death calmly.

"M. Gervasi did not leave me for a moment. He gave me nothing without telling me the reason of it. He had to give me an emetic eight times. No cordials were given, instead he made me drink 200 pints of lemonade. This treatment, which may seem extraordinary to you, was the only way of saving my life. Any other treatment would have brought me to certain death and I am persuaded that most of those who have died of this dreadful illness would be alive today, if they were treated as I was."

The naïve faith in lemonade as a sure cure for smallpox, by the great philosopher of Ferney, is interesting, and on a par with other instances of the same sort, recorded in medical history, concerning those whose profound knowledge would seem a bar to such reasoning.

WM. PEARCE COUES, M.D.

Prouts Neck, Maine.

ARTICLES ACCEPTED BY THE AMERICAN MEDICAL ASSOCIATION COUNCIL ON PHARMACY AND CHEMISTRY

To the Editor: In addition to the articles enumerated in our letter of June 7 the following have been accepted:

Burbot Liver Products Co.
- Rowell's Burbot Liver Oil

Eli Lilly & Co.
- Combined Diphtheria Tetanus Toxoid, Alum Precipitated
- Tablets Carbarsone 0.05 gm. (¾ gr.)
- Tablets Carbarsone 0.25 gm. (3¾ gr.)
- Suppositories Carbarsone 2 gr.

Wm. S. Merrell Co.
- Cod Liver Oil Concentrate Tablets—Merrell

Sharp & Dohme, Inc.
- Staphlylococcus Toxoid—Mulford

Winthrop Chemical Co., Inc.
- Avertin with Amylene Hydrate

PAUL NICHOLAS LEECH, *Secretary.*
535 North Dearborn Street,
Chicago, Illinois.

RECENT DEATHS

PIPER — FRANK PIPER, M.D., of 27 Lancaster Street, Cambridge, died at his home, July 8. He was in his seventy-first year.

Dr. Piper was born in Charlestown, N. H., in 1866, graduated from the Massachusetts College of Pharmacy in 1889 and from the Harvard Medical School in 1893. He then practiced medicine in Boston.

After the World War, Dr. Piper became interested in

medical insurance. He was first associated with the John Hancock Company, later joining the Boston Mutual Life Insurance Company, where he had been medical director for the last seven years.

He held memberships in the American Medical Association, the Massachusetts Medical Society, the American Legion and the Masonic Order.

His widow, Mrs. Blanche Drew Piper, and two nephews survive him.

FRENCH—John Marshall French, M.D., of 2 South Main Street, Milford, died February 27. He was in his eighty-seventh year.

Dr. French graduated from the University of Vermont College of Medicine in Burlington in 1877 and held memberships in the American Medical Association and the Massachusetts Medical Society.

PIGEON — James C. Pigeon, M.D., of 27 Elm Hill Avenue, Roxbury, died recently. He was in his eighty-third year.

Dr. Pigeon graduated from the Harvard Medical School in 1883 and was a retired member of the Massachusetts Medical Society.

HARLOW—Corydon Webster Harlow, M.D., of 59 Ashland Street, Melrose Highlands, died at his home on July 7. He was in his seventy-third year.

Dr. Harlow attended Bates College and received his M.D. degree from Bowdoin Medical School. After practicing in Maine, he went to Melrose. He was a member of the Massachusetts Medical Society.

His widow, Mrs. Alida Harlow, and a daughter, Mrs. Marcella Kerr, survive him.

NOTICES

REMOVALS

Robert L. DeNormandie, M.D., and Delos J. Bristol, Jr., M.D., announce the removal of their offices to 330 Dartmouth Street, Boston.

David Karp, M.D., announces the opening of an office for the summer at 69 B Street, Allerton, Mass.

REPORTS OF MEETINGS

SPECIAL LECTURES IN ENDOCRINOLOGY

Dr. M. O. Lee delivered one of the special lectures in endocrinology at the Harvard Medical School on March 18. His subject was "The Anterior Pituitary Gland and Protein Metabolism."

During the past 50 years it has been repeatedly observed that abnormalities in the anterior pituitary gland are associated with abnormalities in body growth. Deficiency results in dwarfism or cachexia, while hyperactivity causes acromegaly or gigantism. Complete removal of the pituitary causes a cessation of growth and a loss of weight from the soft tissues and viscera, deficiencies which are repaired by injections of extracts or implants of pituitary tissue. The administration of such extracts to normal adult animals greatly accelerates growth processes and causes the development of gigantism.

In the study of growth and protein metabolism, it is essential that true growth be defined. Dr. Lee restricted the term as follows: "True growth is an increase in size and weight as normally exhibited by young animals; or, in adults, an increase in size and weight exhibiting the same chemical and metabolic characteristics as true growth in young animals." There are both metabolic and chemical manifestations of true growth, which may be summarized as follows:

A. Metabolic.
   1. Active manufacture and deposition of body protein.
   2. Positive nitrogen balance and nitrogen retention.
   3. Retention of water and mineral salts.
   4. Slight formation of body fat.
   5. Large food consumption and energy metabolism per unit of body weight.

B. Chemical.
   1. High content of protein.
   2. High content of water and mineral salts.
   3. Low content of fat.

Metabolic and chemical changes also occur with advancing age and maturity.

A. Metabolic.
   1. Zero or slightly positive nitrogen, water and mineral balances.
   2. Low food consumption and energy intake per unit of body weight.

B. Chemical.
   1. Decrease in nitrogen and salt content of the body on a fat-free basis.
   2. Decrease in percentage of water and decrease in the ratio of water to nitrogen.
   3. Increase in percentage of fat, sometimes tenfold or more.

The sine qua non of true growth may be considered as the formation and deposition of body protein, which decreases progressively as the growth curve decreases. This decrease occurs in spite of the fact that the tissues are furnished with a plethora of amino acids. Protein is not stored in the body, and the protein balance in adults is practically zero, anabolic and catabolic processes being equal.

Pituitary principles and hormones are supposed to play an important role in the regulatory mechanisms and homeostatic factors controlling growth processes. Some workers, however, claim that there is no growth hormone present in the pituitary secretions and attribute the actions of such secretions to secondary effects of the thyrotropic hormone and prolactin. It is believed that some of the growth effects of pituitary extracts and pituitary ablation are secondary to changes in the adrenal cortex.

To prove that pituitary hormones are primarily concerned with growth and protein metabolism, it is necessary to demonstrate that they have a specific effect on weight, growth and food consumption, which is abolished by ablation of the pituitary and restored by the injection of extracts. Dr. Lee has conducted experimental work on rats, which has conclusively shown that the growth hormone causes greater growth in animals receiving injections of the principle than that which occurs in litter mates on the same food intake. Opposite conditions occur after hypophysectomy, when the animals lose weight more rapidly than their litter mates which are maintained on the same rations. The changes in growth are separate from the food intake, and there is very little probability that they are secondary to changes in metabolic rate.

Chemical analyses of animals treated with growth hormone showed them to be practically the same as the immature animals before treatment was begun, while the controls showed changes in the direction of chemical ma-

turity. The excess weight gained was composed largely of water, protein and mineral substances, while relatively little of it was fat. Hypophysectomized animals showed a depletion of body proteins with relatively little fat loss, while the controls lost fat and spared the body proteins.

There is a variation in size of organs as well as in total body size in pituitary abnormalities. Thus, there is a splanchnomegalia in acromegalics, and a splanchnomicria in dwarfs and individuals with Simmonds's disease. Such changes are exemplified by the liver, the size of which increases disproportionately in animals treated with growth hormone and decreases markedly in hypophysectomized animals. The ratio between liver weight and body weight is thus increased in animals receiving injections of growth hormone and decreased in hypophysectomized animals. These findings do not indicate a "hepatotropic hormone," but mean merely that the liver reflects the changes in protein metabolism since it is the only source for the production of urea and the deamination of amino acids. The liver also acts as a site of storage for what little protein is stored in the body and is the organ which forms the fibrinogen of the blood. Cytologic studies of the liver in animals treated with growth hormone showed merely an increase in all elements in the same proportion as are normally present. The number of cells per gram of tissue was not increased, and the nuclei were the same in size and character. Analyses of livers in animals receiving the growth principle showed a shift in character toward that of young, actively growing animals, as there was an increase in nitrogen, protein, water and mineral salts, and a decrease in fat.

A study of the nitrogen and mineral balances in animals treated with growth hormone showed that they were strongly positive. Nitrogen retention was very marked, in some instances amounting to 50 per cent in 2 or 3 days. This accounts for the reduction in the production and excretion of urea observed in these animals. Ablation of the pituitary results in an increase in the amount of nitrogen excreted. Teeland Watkins found that injections of the growth hormone caused a decrease in the blood nonprotein nitrogen and blood urea amounting to 50 per cent in some cases. Schaffer, Lee and Ayres have shown that significant changes in the nitrogen partition of the tissues themselves occur as a result of growth hormone treatment and after hypophysectomy. Normally the nonprotein nitrogen is maintained very constant, regardless of the intake, although in pregnant women and children it is subject to some variation. In the latter individuals there is an increase in the anterior pituitary activity, which probably accounts for the variations observed. The concentrations of albumin, globulin, creatinine, creatine and uric acid are not specifically influenced by the growth hormone. Glutathione, however, is markedly increased in the liver and muscle following even a single injection of the principle, although the changes are not proportional to the dose injected. Hypophysectomy and the injection of growth hormone produce no significant change in the endogenous protein metabolism. The anabolic action of the growth hormone is thus believed to be due to its effect on the exogenous protein metabolism. At least a portion of the excess protein retained is in a labile form and subject to prompt catabolism. The lability of these proteins is greatest during the first part of the treatment and decreases as treatment is continued. These proteins first fill the reserve depots and are only gradually converted to more stable tissue. The growth hormone thus acts by replenishing the protein stores and by furnishing a plethora of stored protein to serve as a source for more stable proteins. No chemical difference is implied between the body structural proteins and the "labile" proteins.

Similarities of nitrogen metabolism are noted in certain clinical and experimental conditions:

A. A positive nitrogen balance, a deposition of body protein, an increase in body weight and low values of blood nonprotein nitrogen and amino acids are noted in the following conditions:
   1. The normal growth period in infancy and childhood.
   2. The growth period of the latter months of pregnancy.
   3. The period of developing acromegaly.
   4. Recovery from febrile diseases.
   5. Recovery from fasting.
   6. Experimental treatment with pituitary growth hormone.

B. The opposite conditions — negative nitrogen balance, loss of accumulated proteins, increase in blood urea, nonprotein nitrogen and amino acids, and loss of body weight— prevail during:
   1. The puerperium.
   2. The period of developing pituitary cachexia.
   3. Certain types of malnutrition.
   4. Experimental hypophysectomy.

NEW ENGLAND PHYSICAL THERAPY SOCIETY

At the annual meeting of the New England Physical Therapy Society held at the Hotel Victoria, Boston, on Wednesday evening, May 26, the following officers were elected: president, Hosea W. McAdoo, M.D., Arlington; first vice-president, George B. Carr, M.D., Lynn; second vice-president, Henry A. Tadgell, M.D., Wrentham; secretary, William D. McFee, M.D., Boston; treasurer, Franklin P. Lowry, M.D., Newton; councilors for three years, Claude L. Payzant, M.D., Boston, and William G. Curtis, M.D., Wollaston.

Dr. Charles Whelan of Boston, guest speaker of the evening, addressed the society on "X-Ray and Radium Therapy."

GUILD OF ST. LUKE

The annual meeting of the Guild of St. Luke was held at the Carney Hospital, South Boston, on Wednesday, June 23, through the courtesy of the staff and of the Sisters of Charity in charge of the hospital.

The surgical and orthopedic staffs, including Drs. W. E. Browne, A. McK. Fraser, L. E. Phaneuf and A. R. MacAusland, performed a variety of operations; visits to the medical wards were conducted by Dr. L. F. Curran; and scientific papers were presented by other members of the staff.

The following named officers were elected for the ensuing year: president, Dr. Louis F. Curran; vice-president, Dr. Frederick W. O'Brien; treasurer, Dr. Edward L. Kickham; secretary, Dr. Daniel L. Lynch; councilors, Drs. Charles E. Mongan, Brainard F. Conley, James J. Regan, Norman A. Welch and John F. Casey.

AMERICAN INSTITUTE OF HOMEOPATHY

The ninety-third annual convention of the American Institute of Homeopathy at the Hotel Statler, June 13 to 17, was attended by over 450 members from every state in the Union. The general meetings were presided over by Dr. C. S. Smith, of New Haven, president, and the

local committee on arrangements was in charge of Dr. R. W. Spalding, of East Dedham.

A public health meeting on the evening of June 14 was held under the chairmanship of Dr. Winfred Overholser, former Massachusetts commissioner of mental diseases. Addresses were given by Dr. H. D. Chadwick, Massachusetts commissioner of public health, Mr. W. H. MacDonald, associate director of public health of New Jersey, and Dr. N. E. Paine, of West Newton, an 83-year-old veteran in homeopathic practice, who has been chairman of the board of trustees of the Westboro State Hospital for many years.

The scientific sessions consisted of meetings of the Bureau of Public Health; Bureau of Homeopathy; Surgical, Gynecological and Obstetrical Society; Bureau of Drug Pathogenesis; Bureau of Clinical Medicine; National Society of Physical Therapy; Ear, Nose and Throat Bureau; and Eye Bureau.

The annual banquet was held on the evening of June 16. Dr. John Sutherland, of Boston, acted as toastmaster. The speakers included Dr. C. A. Burrett, dean of New York Medical College, Dr. W. A. Pearson, dean of Hahnemann Medical College of Philadelphia, and Dr. L. C. Hertzog, of Chardon, Ohio. Dr. J. B. Gregg Custis was inducted into office as the new president of the Institute.

SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING MONDAY, JULY 19

WEDNESDAY, JULY 21—

†12 m. Clinicopathological conference. Children's Hospital Amphitheater.

FRIDAY, JULY 23—

12 m. Massachusetts General Hospital. Clinical meeting of the staff of the Children's Medical Service. Ether Dome.

SATURDAY, JULY 24—

*10 a. m. - 12 m. Staff rounds at the Peter Bent Brigham Hospital. Conducted by Dr. Robert T. Monroe.

*Open to the medical profession.
†Open to Fellows of the Massachusetts Medical Society.

SEPTEMBER 13-17—Fifth International Congress of Radiology. Page 709, issue of April 22.

OCTOBER 1 and 2—New England Surgical Society. Providence, R. I.

OCTOBER 5-8—American Public Health Association meeting. New York City.

OCTOBER 9—American Board of Ophthalmology, Chicago. Page 722, issue of April 22.

OCTOBER 19, 20, 21—Academy of Physical Medicine. Page 723, issue of April 22.

OCTOBER 25-29—American College of Surgeons. Chicago, Illinois.

NOVEMBER 1-12—1937 Graduate Fortnight of the New York Academy of Medicine. Page 1000, issue of June 3.

APRIL 4-8, 1938—The American College of Physicians. Page 41, issue of July 1.

BOOK REVIEWS

THE INTELLECTUAL FUNCTIONS OF THE FRONTAL LOBES. A Study Based upon Observation of a Man After Partial Bilateral Frontal Lobectomy. Richard M. Brickner. 354 pp. New York: The Macmillan Company, 1936. $3.50.

By his intensive study of a patient from whom the major portion of both frontal lobes of the brain had been operatively removed, Dr. Brickner has been able to make observations, upon a human being, which are unique in respect to the conditions presented. It is difficult to conceive of any more comprehensive or detailed description of the intellectual and psychologic processes involved than those which the author has so carefully related.

The book is divided into three parts, the first of which concerns the patient's history previous to Dr. Brickner's period of observation, a careful account of the operation together with the amount of brain tissue removed, and also a background of the patient's earlier life as a contrast to the observations which follow.

Part two is the detailed and systematized account of the patient's intellectual status as observed by daily contact and careful periodic neurologic and psychologic examinations during the course of a year. The author points out that certain symptoms in the intellectual sphere have an emotional coloring, and others do not. The former are concerned largely with lack of restraint as indicated in various ways—that is, by impairment in controlling emotion, by boasting, by self-aggrandizement, by mild evidences of hostility, and the like. The patient's impairment of restraint in the emotional sphere was one of the outstanding evidences of abnormality. His reactions were repeatedly childlike both in the lack of ordinary restraint in speech and in occasional puerile hostility. Any evidences of the preservation of restraint were slight and few in number.

The intellectual symptoms without an emotional coloring were concerned mainly with difficulty in associating and synthesizing what the author calls mental "engrammes," in maintaining fixation and attention, and with an inability to particularize. Retention of memory for recent events was severely impaired, but was relatively unimpaired for events several years previously. There was great difficulty in remembering names. The patient showed almost total inability to grasp the meaning of complex sentences or thought processes. His learning capacity was extremely slight, and complicated by marked distractibility. Other phenomena were the lack of insight into the gravity of his condition and an almost constant euphoria associated with *Witzelzucht*. There was no real aphasia, as the left frontal lobe had been resected anterior to Broca's area. There was, however, marked preservation. Throughout the whole description of the patient one is impressed with the idea that his intelligence and actions were those of a silly, spoiled child.

In the interpretation of the picture presented in part three it may be well to quote from Dr. Brickner's summary. He believes that none of the patient's symptoms indicate "an alteration in the fundamental nature of any mental process, but only the impairment of its completeness. Hence the changes are fundamentally not qualitative but quantitative in nature. . . . Only one function is considered as primarily affected. This is the elaborate association or synthesis with complex structures of the simpler engrammic products associated in the more posterior parts of the brain."

As Dr. Frederick Tilney says in his excellent preface to the book, Dr. Brickner has provided "the record of a unique case which cannot fail to be of lasting service to neurologists, psychiatrists and psychologists." He might have added with equal truth—to neurosurgeons!

TEMPLE UNIVERSITY OBSTETRICAL GUIDE-BOOK. J. O. Arnold. 197 pp. Philadelphia: Corson Publishing Company, 1937. $2.50.

It is difficult to classify this obstetric guidebook as it combines instructions for nurses, for students and for interns with a section of 40 pages regarding the "Temple treatment" of eclampsia, including a reprint from the *Medical Clinics of North America* and a presentation of case reports adapted to student teaching. The book contains a great deal of really valuable material especially Part II, which gives a clear account of the treatment of

eclampsia by means of water-balance control. Parts I and III are elementary, but contain much that is worth while. There is no index, which makes it difficult to use the book for reference.

The author states that the book has been published because of a demand for the small obstetric booklet which he had formerly used in his clinic and which is now out of print. To quote his own words, "It is, of course, in no sense a textbook. Nor is it a compendium of hospital rules and regulations, but rather the setting forth, in such condensed and concrete form and application as to be always readily available, just what may be most often needed in everyday obstetrical practice—in the home as well as in the hospital. The little volume was not planned or premeditated. Topsy-like, 'it just growed,' and it makes no pretensions to more than the humblest place in the illustrious family of obstetrical books."

THE OCULAR FUNDUS IN DIAGNOSIS AND TREATMENT. Donald T. Atkinson. 142 pp. Philadelphia: Lea & Febiger, 1937. $10.00.

This book gives a short outline of the general characteristics of the ocular fundus with their practical application in health and disease. It is intended for use by neurologists, surgeons, diagnosticians, and so forth, as well as ophthalmologists.

The text is adequate but rather brief for the amount of ground covered. This objection, however, would apply to almost any book of this sort. The illustrations are by the author. The colored plates are rather disappointing since, in a good many instances, the colors are not good and there is a lack of fine detail.

AIDS TO PATHOLOGY. Harry Campbell and Kenneth Campbell. Seventh Edition. 263 pp. Baltimore: Williams & Wilkins Co.; and London: Baillière, Tindall & Cox, 1936. $1.50.

The seventh edition of this little handbook compacts the bare essentials of pathology into 263 pages. Useless as a text or a reference book, it has some value from the standpoint of a quiz or review compend. The use, however, of a considerable number of English terms that are not commonly utilized in this country impairs somewhat its value for this purpose. The classification of tuberculosis, for example, varies from that in general use here, as does the classification of renal diseases.

STARLING'S PRINCIPLES OF HUMAN PHYSIOLOGY. Edited and Revised by C. Lovatt Evans. The chapters on the central nervous system and sense organs revised by H. Hartridge. Seventh Edition. 1,096 pp. Philadelphia: Lea & Febiger, 1936. $8.75.

This seventh edition of Starling's "Principles of Human Physiology" needs no praise to stimulate the appreciation of those who have made use of the former editions. The editor and reviser, C. Lovatt Evans and his associate, H. Hartridge, who is responsible for the chapters on the central nervous system and the sense organs, have maintained the high standard of excellence that has characterized the previous editions.

Practically every chapter has been revised and many of the sections have been rewritten, in spite of the fact that the sixth edition appeared only three years ago; and still the actual length of the text has been reduced. References, which appeared for the first time in the sixth edition, have been continued and are adequate, although, at times, they appear sparse and fairly well limited to the papers of English workers.

The book can be highly recommended to the serious student of physiology and to the physician who is interested in learning about the modern concepts of human physiology.

THE PRINCIPLES OF BACTERIOLOGY AND IMMUNITY. W. W. C. Topley and G. S. Wilson. Second Edition. 1,645 pp. Baltimore: William Wood & Company, 1936. $12.00.

The value of Topley and Wilson's "Principles of Bacteriology and Immunity" can be judged from its popularity. First published in 1929, it was reprinted in 1931, 1932 and 1934. The book was originally planned as a textbook and reference book for the bacteriologist, rather than the medical student, and well fulfilled its purpose, according to the reviewer. In a branch of science, such as bacteriology, that has made and is making rapid progress, it is extremely difficult, if not impossible, to present adequate facts and the proper point of view by mere revision of a previously published text. In their first edition the authors had the advantage of being able to give modern data and concepts that were not limited or prejudiced by former text, and made excellent use of their opportunity.

The second edition follows the general division of the first. Several chapters have been added and some have been omitted. Almost all the chapter headings in Part III, which deals with infection and resistance, have been changed, and although essentially the same material is included, the subject matter has been rearranged. In Part IV, which concerns the application of bacteriology to medicine and hygiene, the section relating to virus diseases has been enlarged from one to four chapters. All this has increased the text by over 300 pages.

The revision has been meticulously done, and the text is thoroughly up-to-date. For example, the chapter dealing with streptococci contains a fairly detailed description of Lancefield's classification, and treatment with "prontosil" is even mentioned in a later chapter on diseases caused by hemolytic streptococci. At the end of the former are over 270 references, and more than a third of these appeared in the literature subsequent to the first edition!

The authors have combined the original two volumes into one. This, to the reviewer, is a distinct disadvantage, for the present edition is far too bulky for easy reference. Notwithstanding, the book cannot be recommended too highly as a textbook to advanced students in bacteriology and as a reference book to workers in bacteriologic laboratories.

AIDS TO DIAGNOSIS AND TREATMENT OF DISEASES OF CHILDREN. F. M. B. Allen. Seventh Edition. 329 pp. Baltimore: Williams & Wilkins Co.; and London: Baillière, Tindall & Cox, 1937. $1.50.

As stated by the author this volume is intended to be of service to students and practitioners. It is in no sense a complete textbook on pediatrics, but is a very excellent summary and should be of great assistance to students prior to examination, as well as to general practitioners who wish to brush up on the subject of pediatrics.

The author's treatment of the diseases and care of the newborn infant is particularly good and indicates that he speaks from a considerable background of practical experience. The suggestions as to the treatment of various medical conditions in childhood are very modern and entirely in keeping with practice in this country.

The reviewer is glad to be able to recommend this volume as an excellent summary of the practical aspects of pediatrics.